The Evolving Epidemiology of HIV Infection in Persons who Inject Drugs: Lessons Learned from Indiana 2015

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2019 HIV•STD•TB•Viral Hepatitis Symposium

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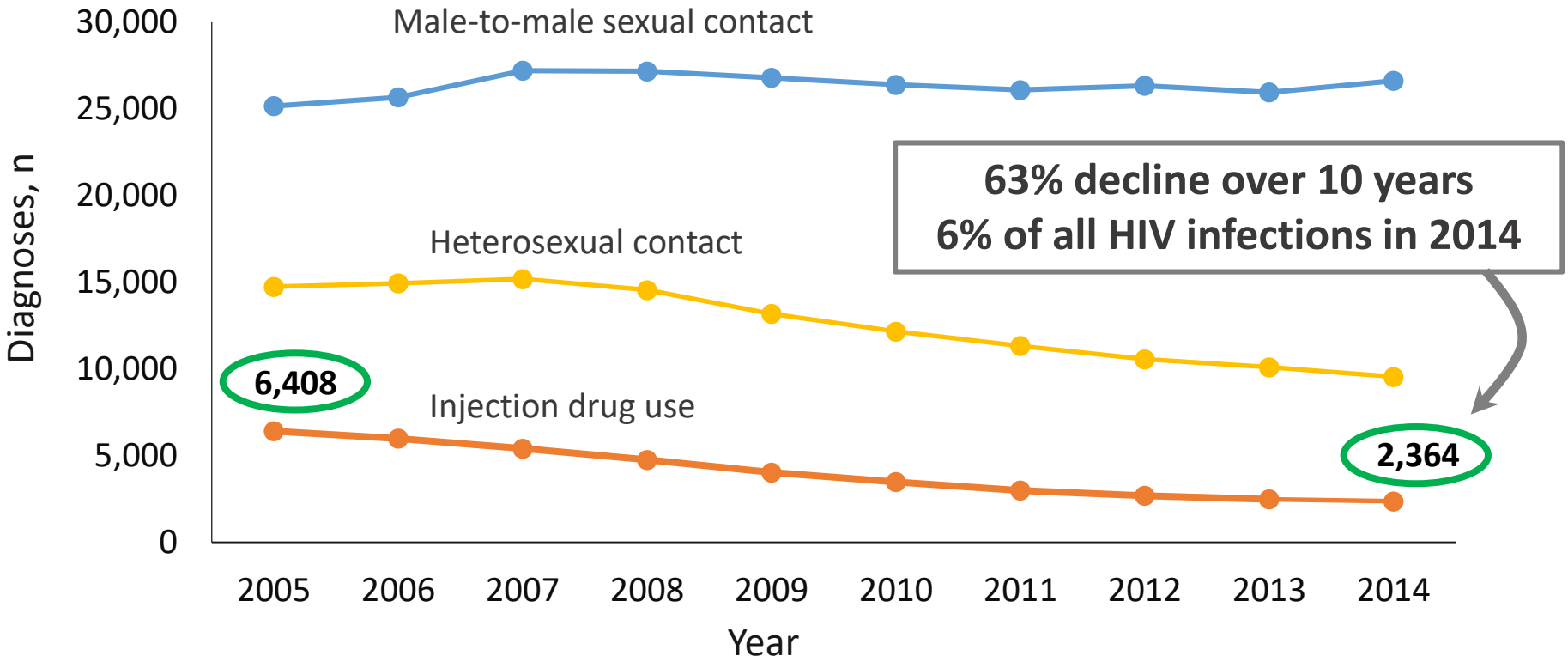
Dr. Brooks has no relevant financial affiliations to disclose

Number of HIV Infections Diagnosed among Adults and Adolescents, by Transmission Category, 2005–2014 - United States and 6 Dependent Areas



CDC National HIV Surveillance System data

Indiana HIV Outbreak: Geography

Scott County pop. 24,000; Austin city pop. 4,200

Single strain of HIV spread rapidly within a dense network of persons who inject drugs (PWID) who were using the prescription opioid oxymorphone

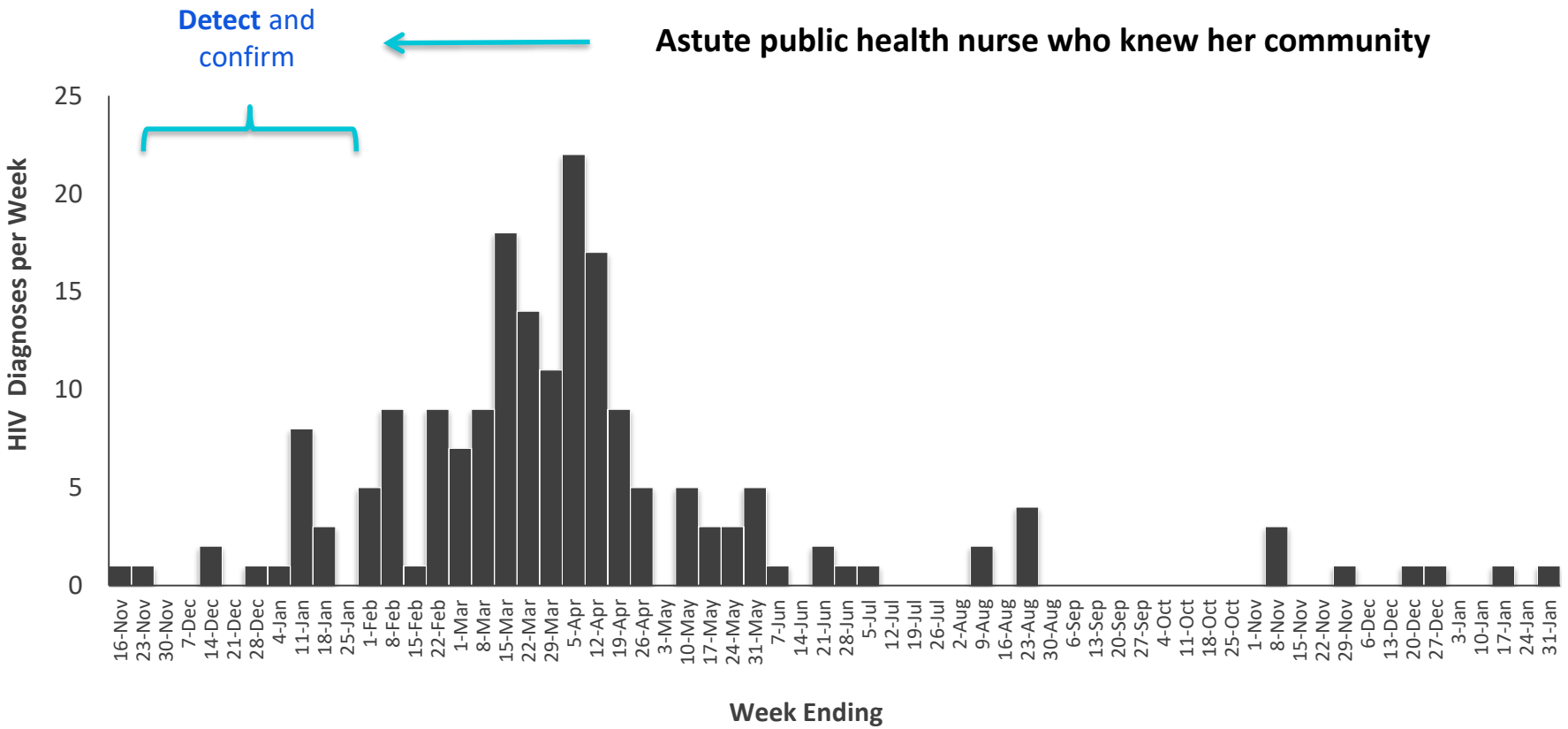
215 HIV Infections diagnosed as of March 2, 2017

Scott County ranked 92nd in many health and social indicators among Indiana's 92 counties

- **Lowest life expectancy**
- **9% unemployment**
- **19% poverty**
- **21% no high school**
- **Many uninsured**

Peters P et al., N Engl J Med 2017;375(3):229-39

HIV Diagnoses by Week, Indiana HIV Outbreak (N=188)



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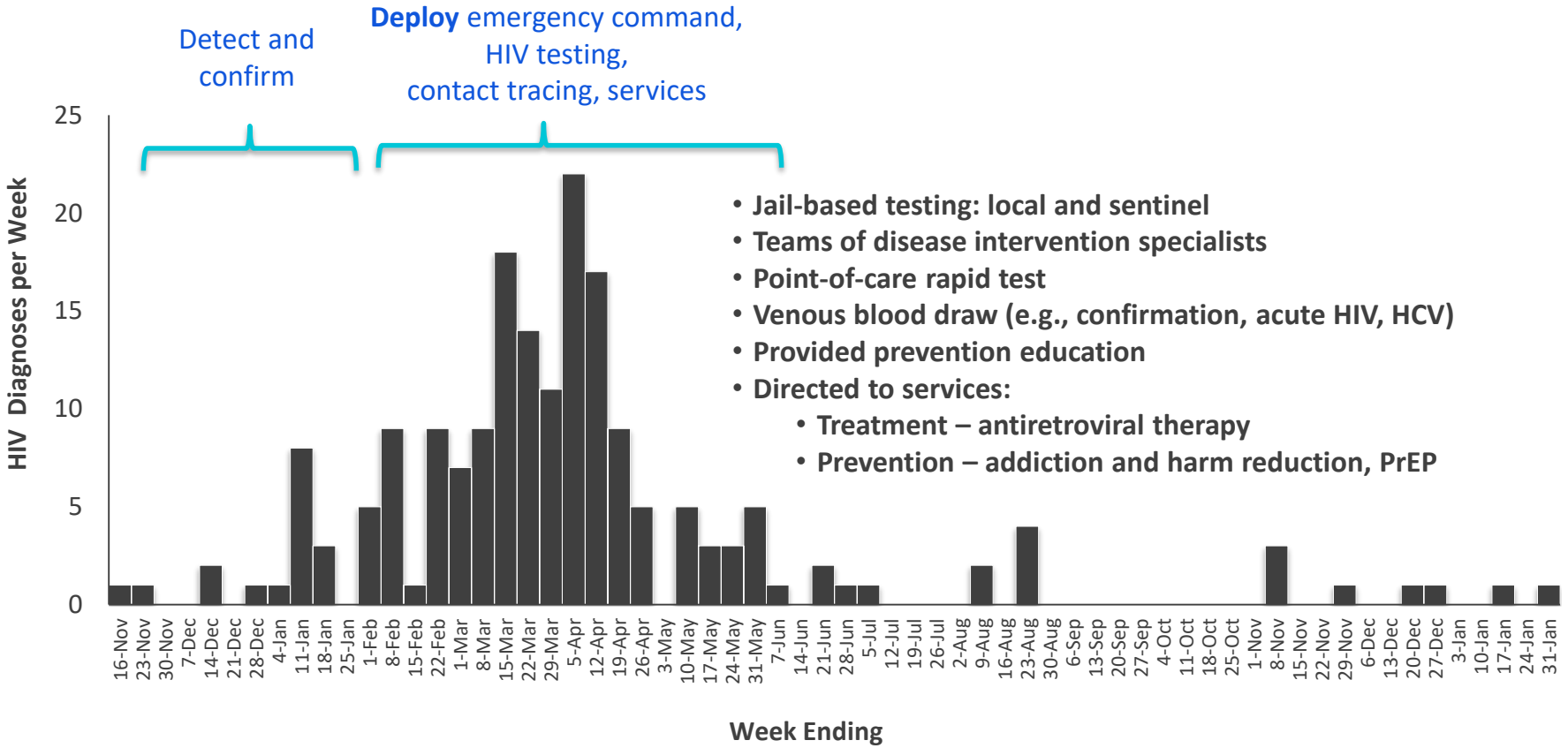

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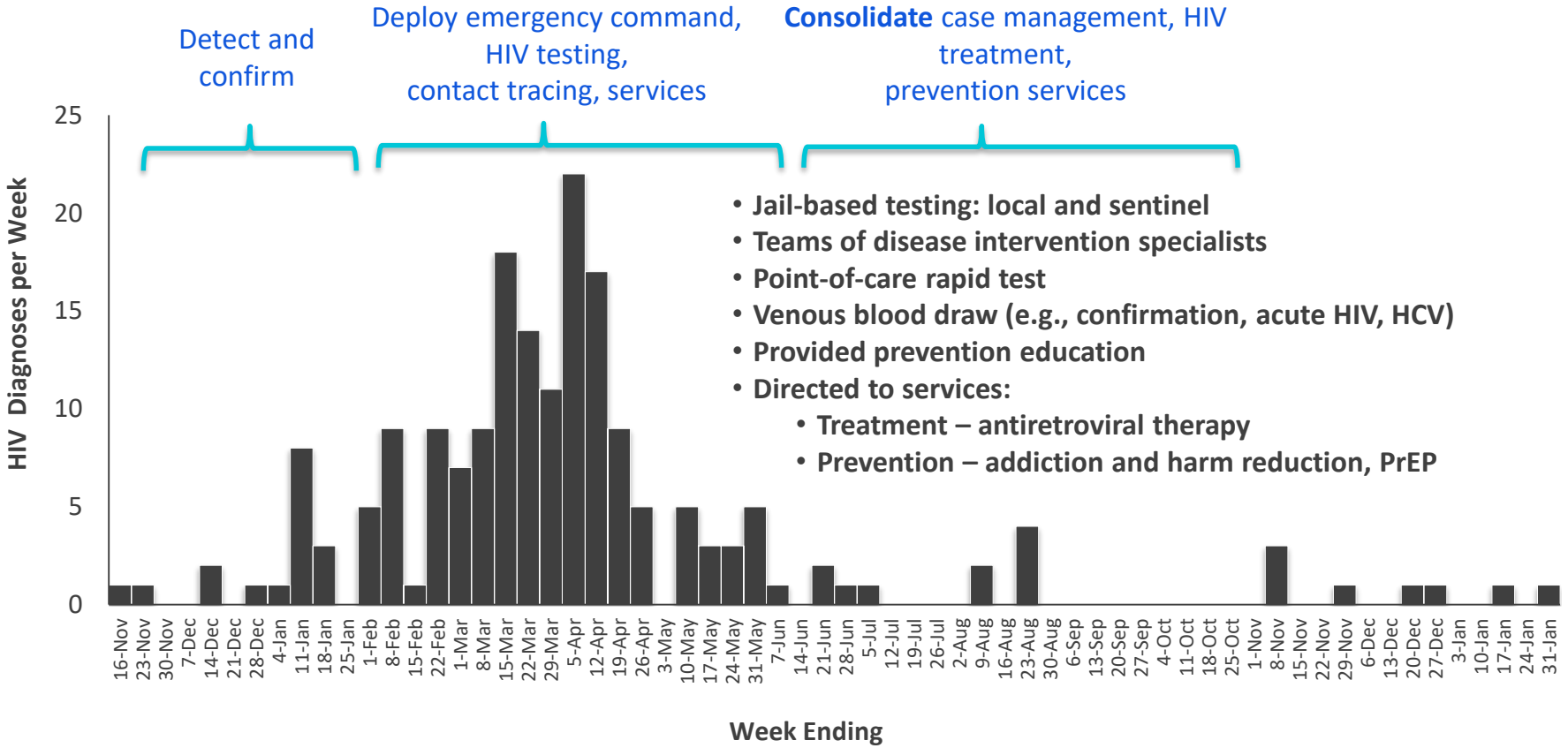

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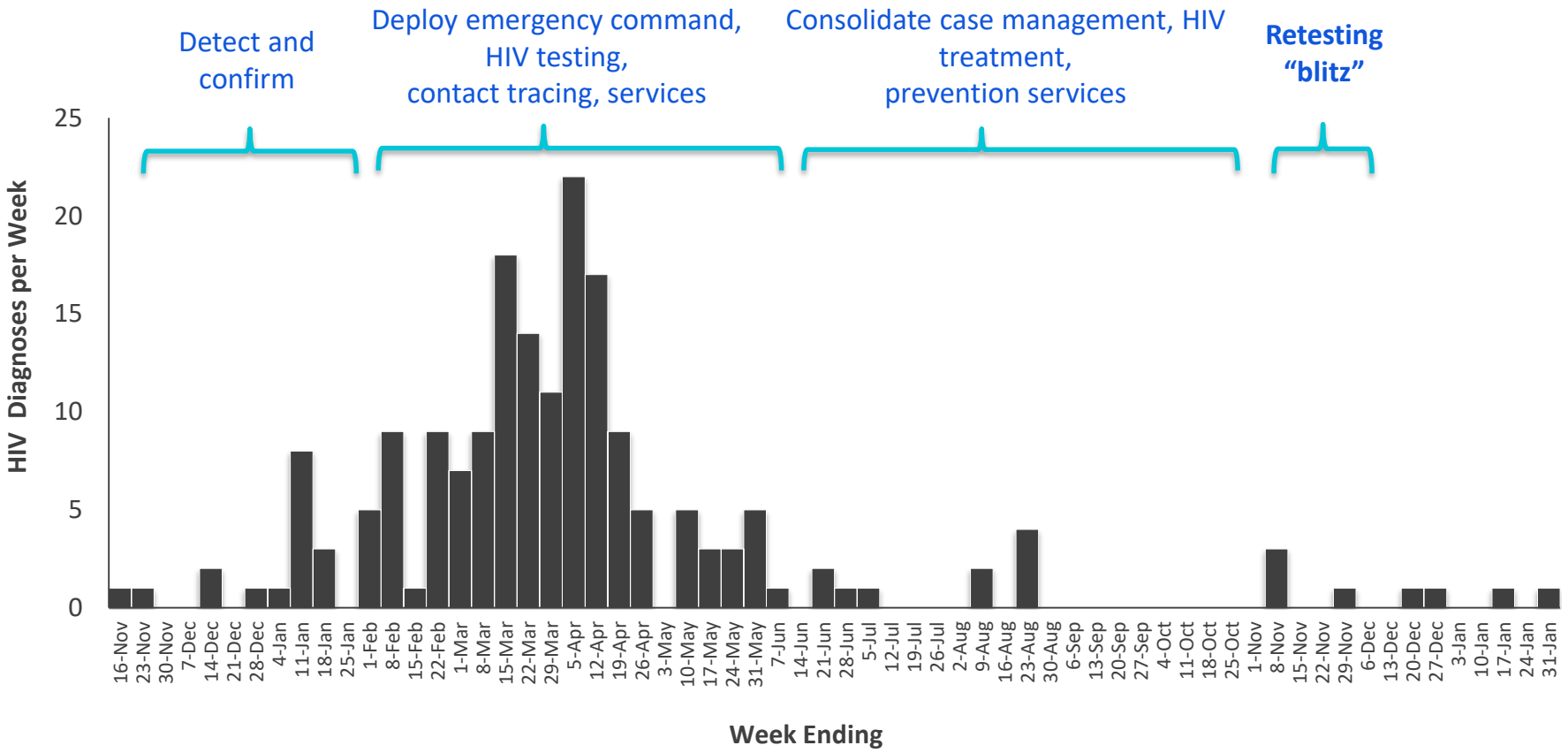

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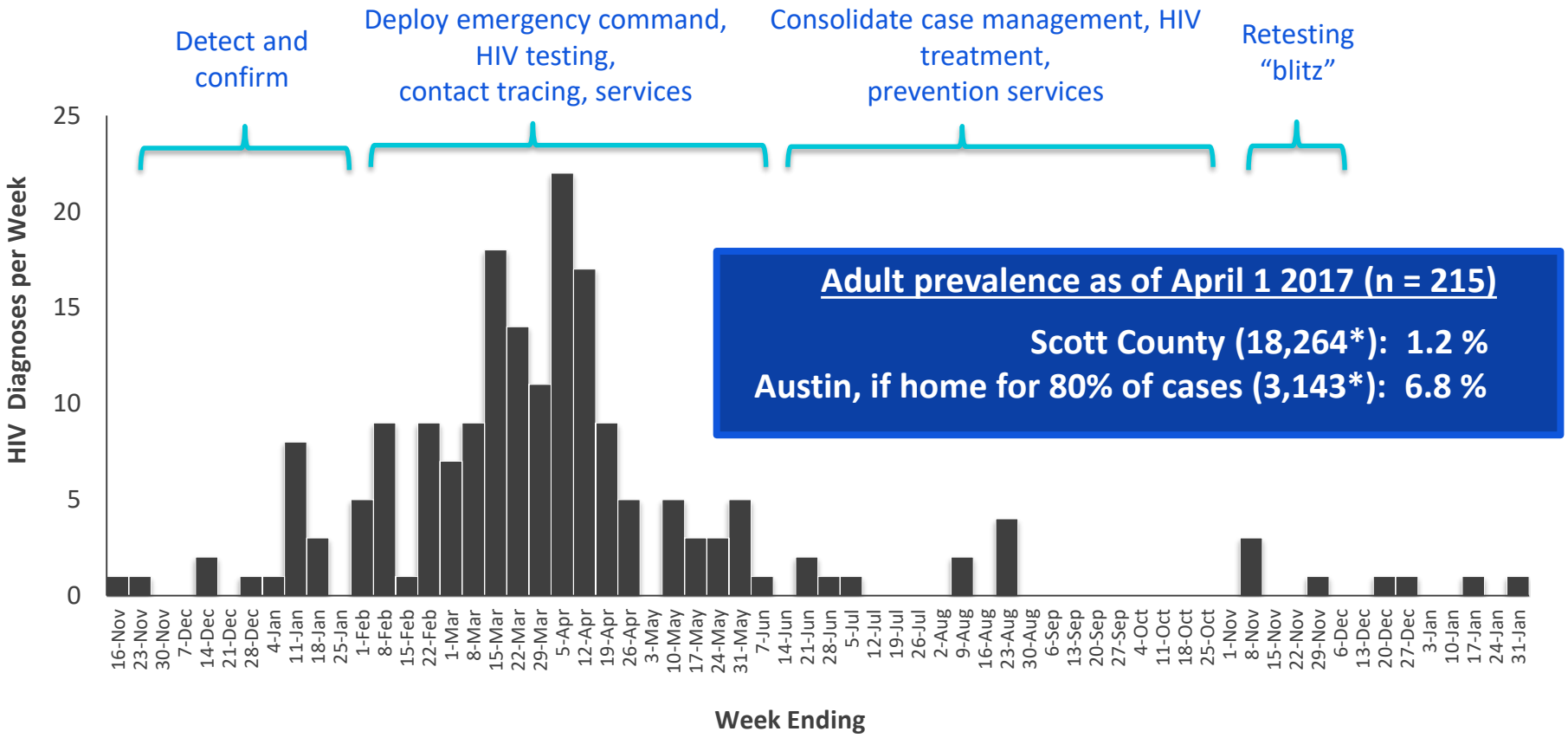

Adult prevalence as of April 1 2017 (n = 215)

Scott County (18,264*): 1.2 %

Austin, if home for 80% of cases (3,143*): 6.8 %

Peters P et al., N Engl J Med 2017;375(3):229-39.

*estimated population age ≥18 years, U.S. Census

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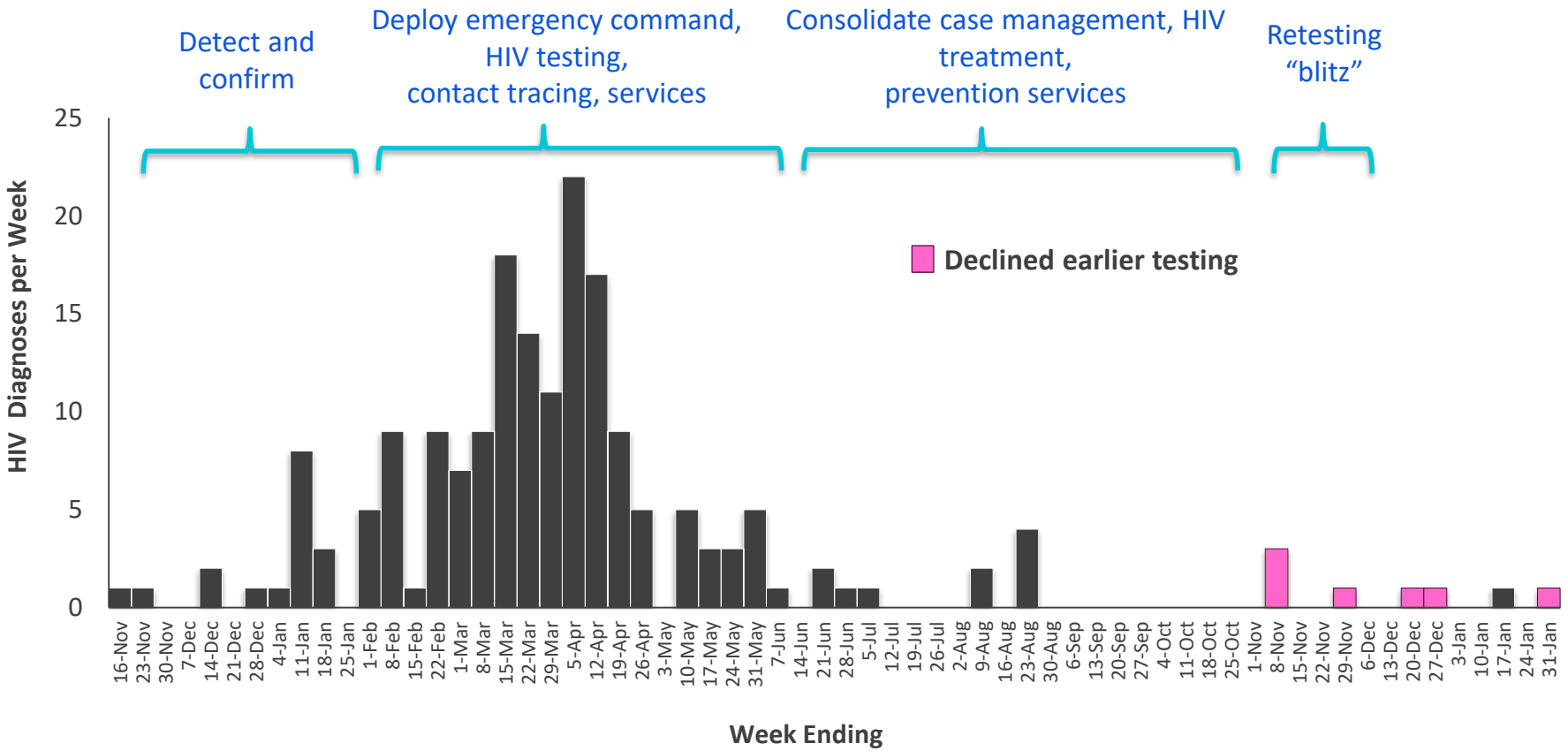

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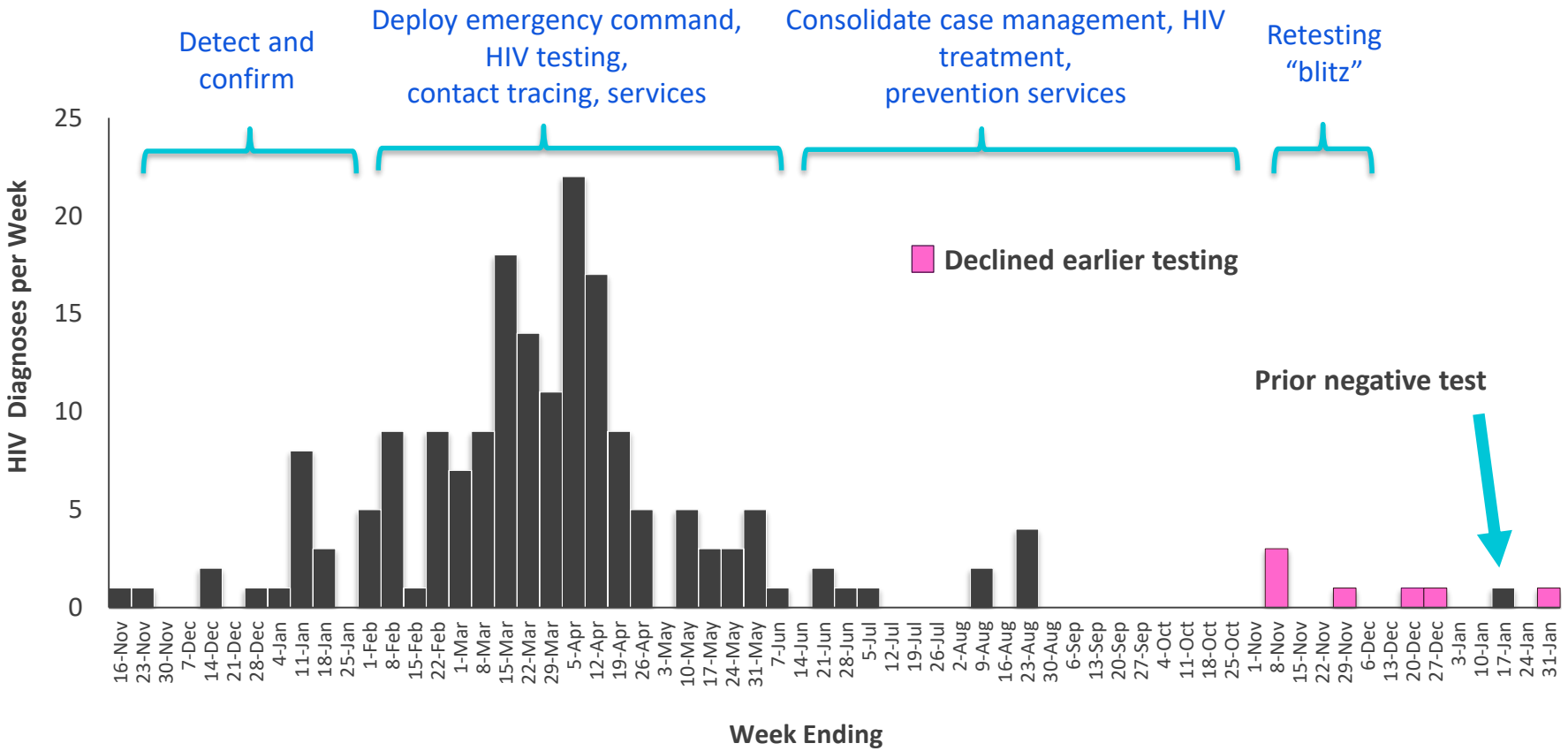

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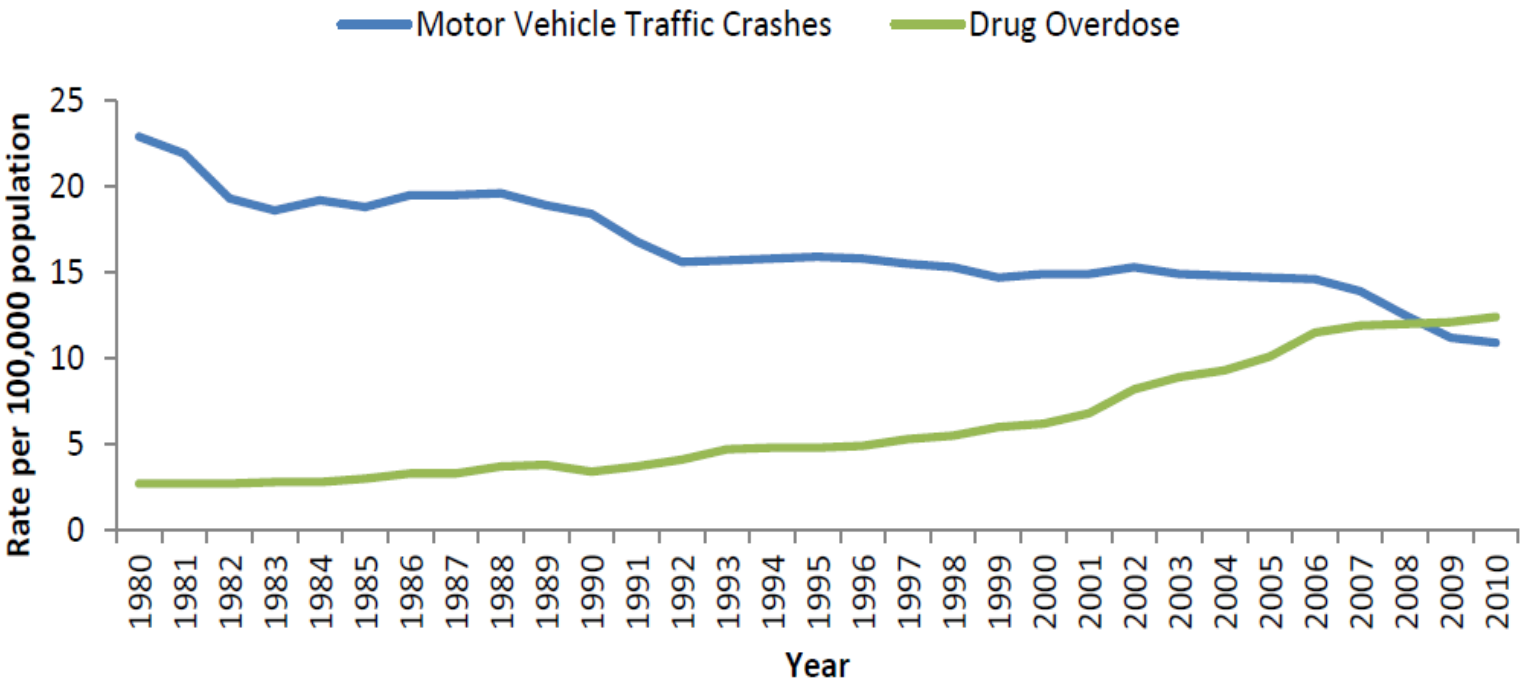
Why Did this Event Happen?

What Had Changed?

Time Magazine, June 15, 2015

Rates of motor vehicle traffic and drug overdose deaths, United States 1980-2010



Source: DHHS, Addressing Prescription Drug Abuse in the United States Current Activities and Future Opportunities , September 2013

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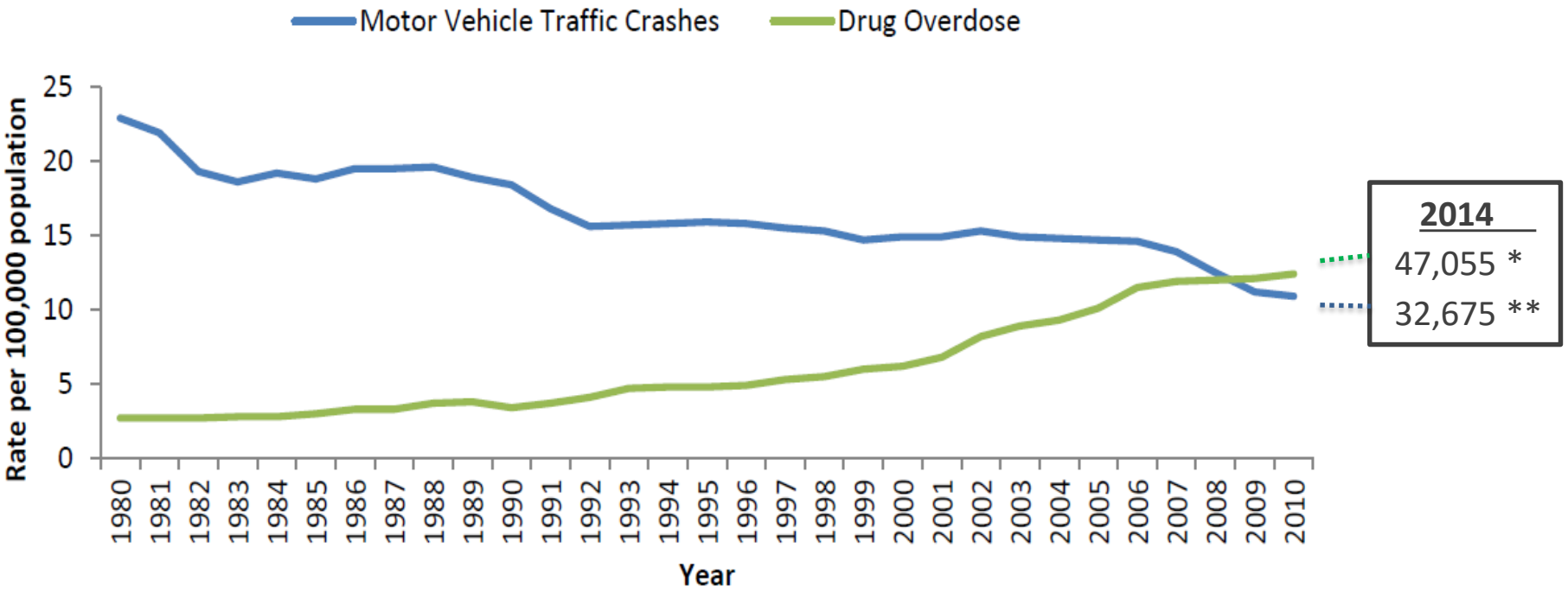

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* MMWR Wkly Rep 2016, 64(50): 1378-82 **http://www-nrd.nhtsa.dot.gov/Pubs/812219.pdf

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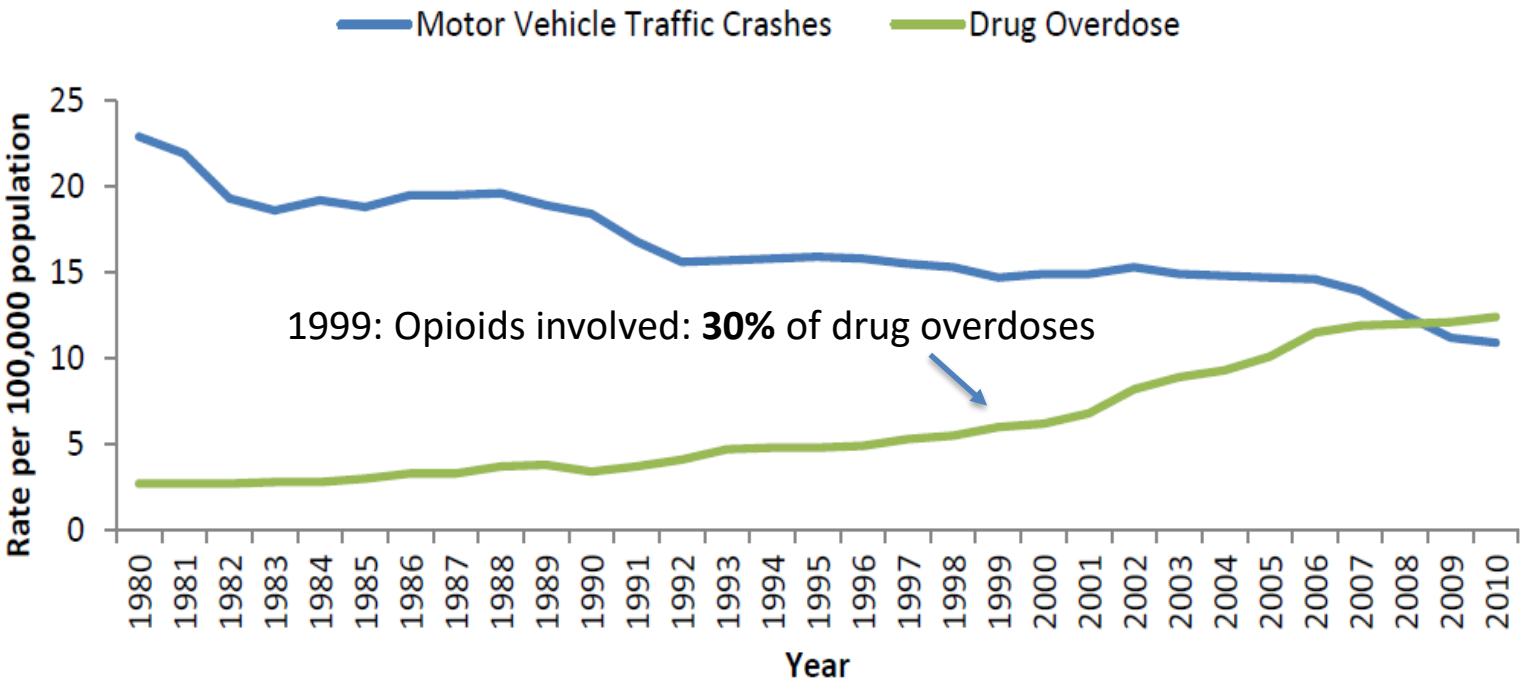

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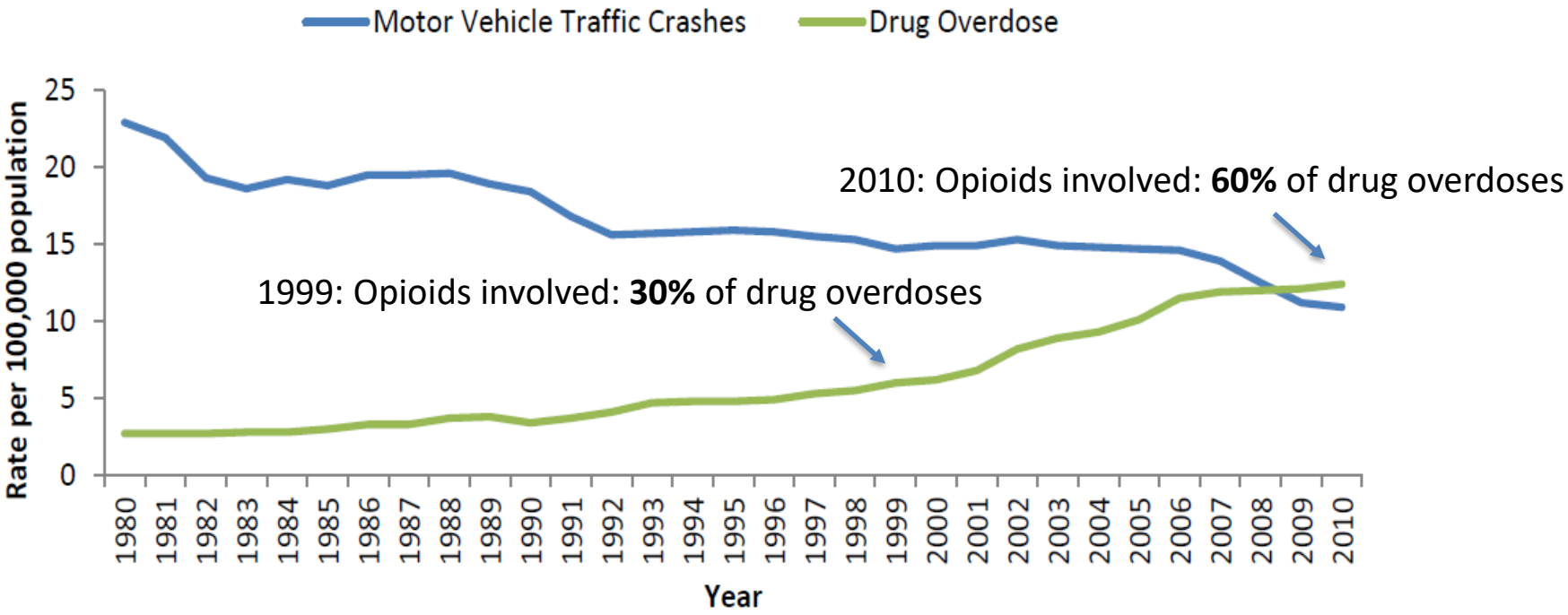

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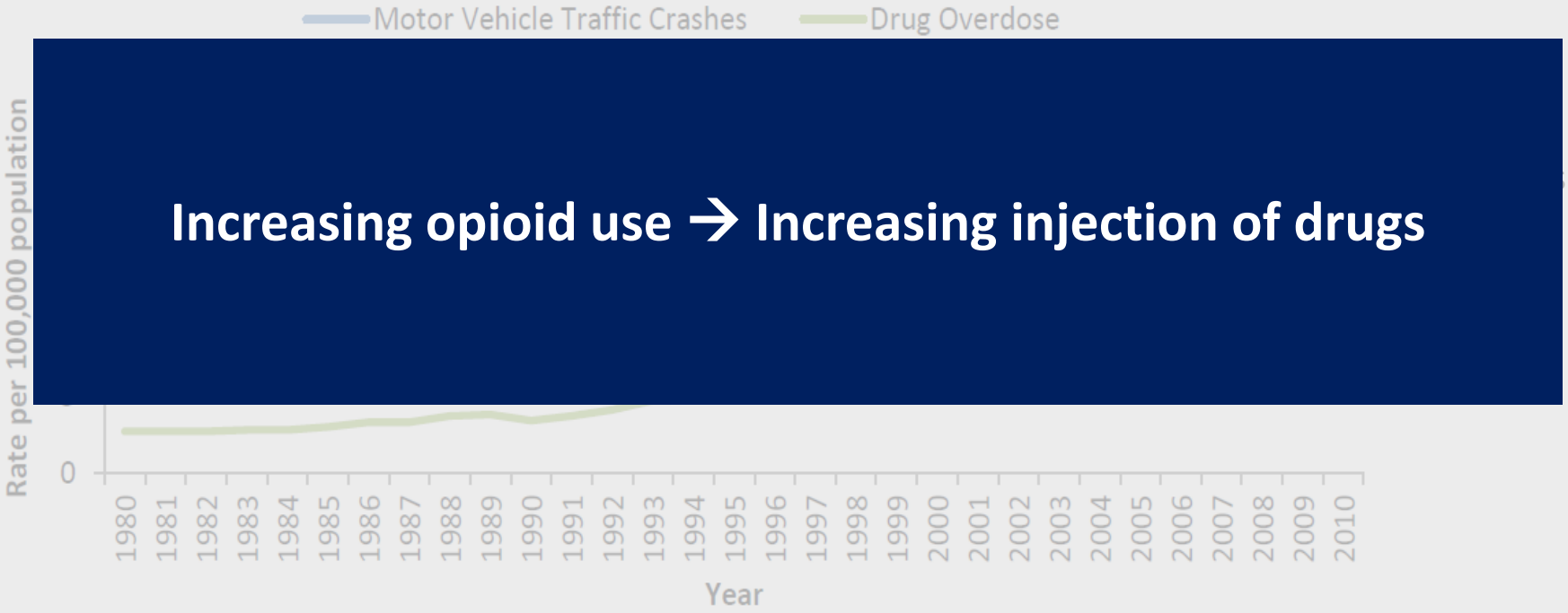


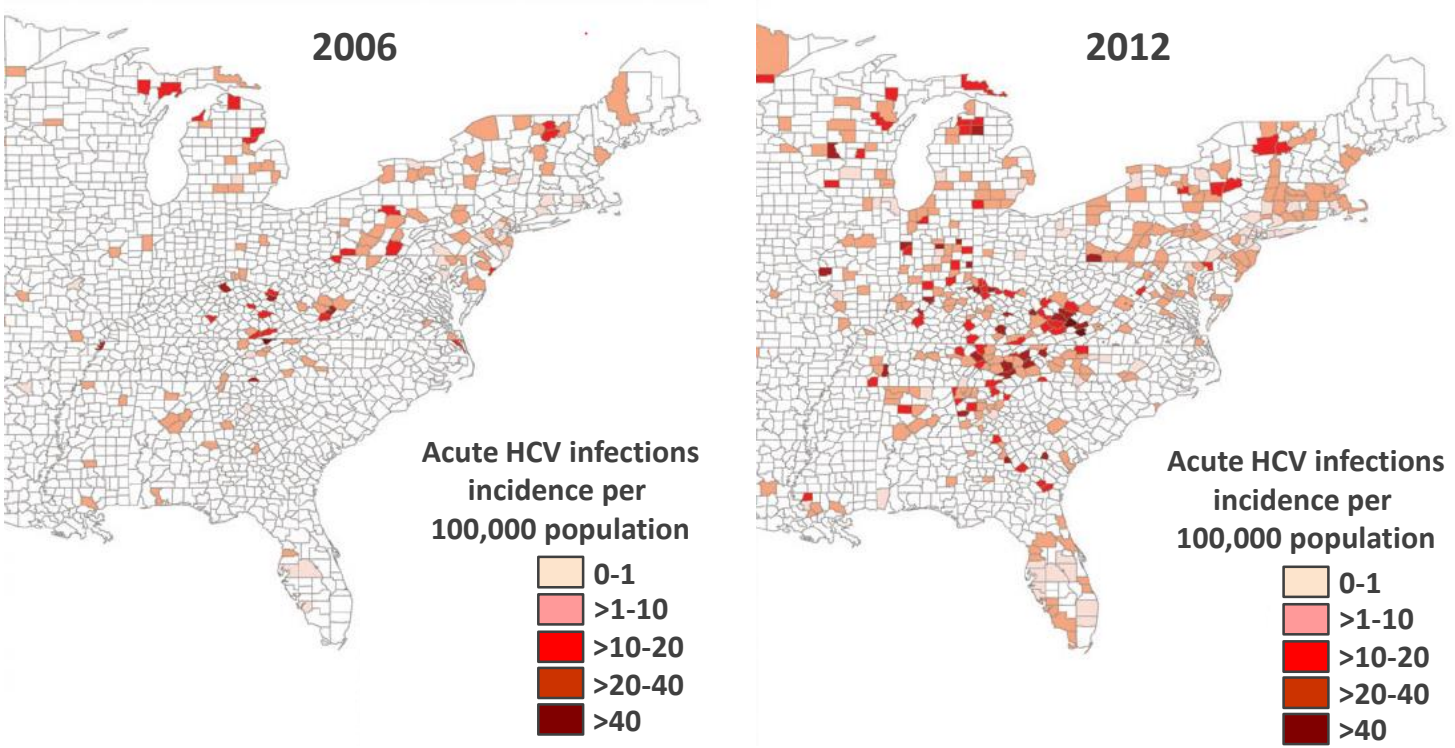
Increasing opioid use → Increasing injection of drugs

Source: DHHS, Addressing Prescription Drug Abuse in the United States Current Activities and Future Opportunities , September 2013

Where is Unsafe Injection Drug Use Occurring and Who is it Affecting ?

- Difficult to assess in the absence of robust surveillance
- Injection drug use is a stigmatized and often criminalized behavior
- However, incidence of acute HCV infection can serve as the "footprints" for unsafe injecting behavior
  - HCV is highly transmissible through and associated with non-sterile injection of drugs
  - The acute phase HCV infection is closely linked in time/space to non-sterile injection (i.e., it's a marker of unsafe injection)

Rapid expansion of injection drug use heralded by epidemic of new HCV infections in areas with historically low rates of HIV infection



Suryaprasad, 2014 Clin Infect Dis;, 59(10):1411-1419

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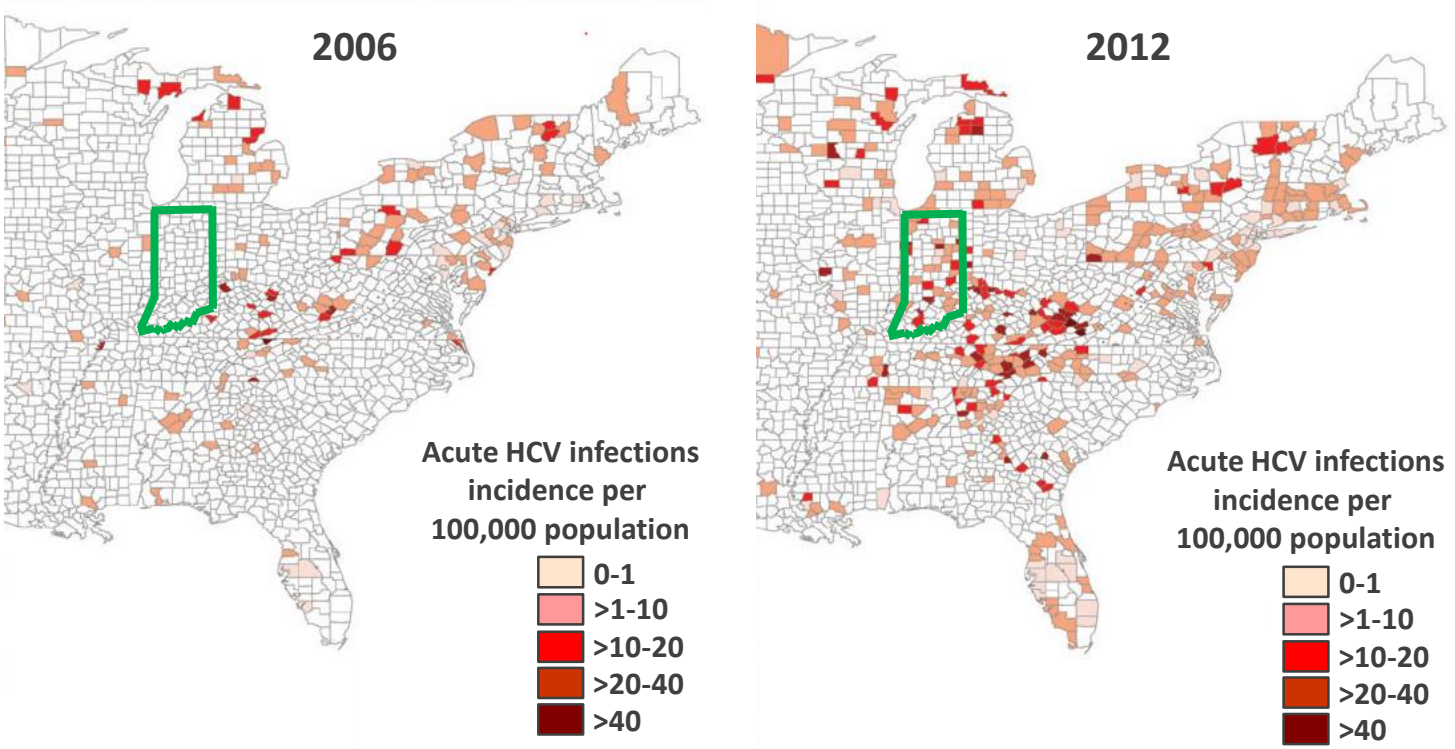

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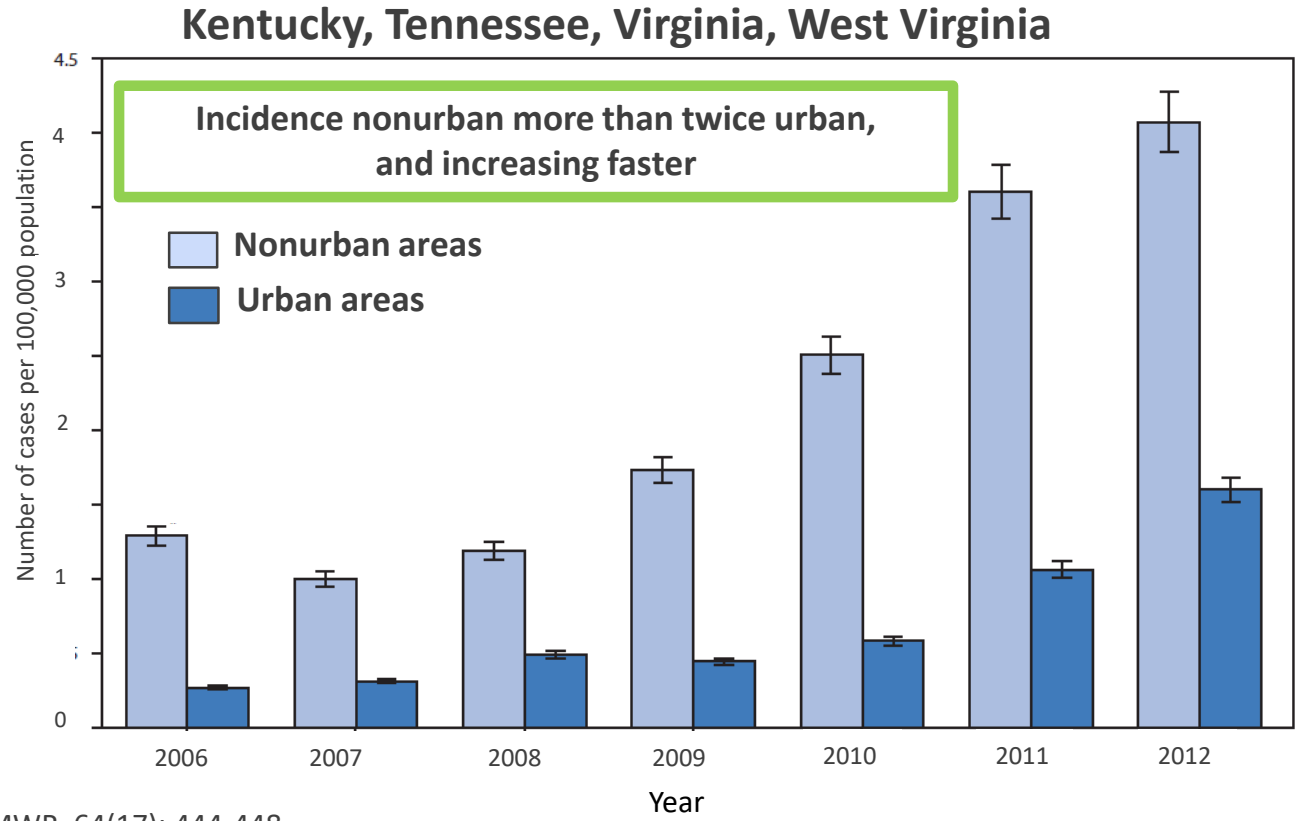
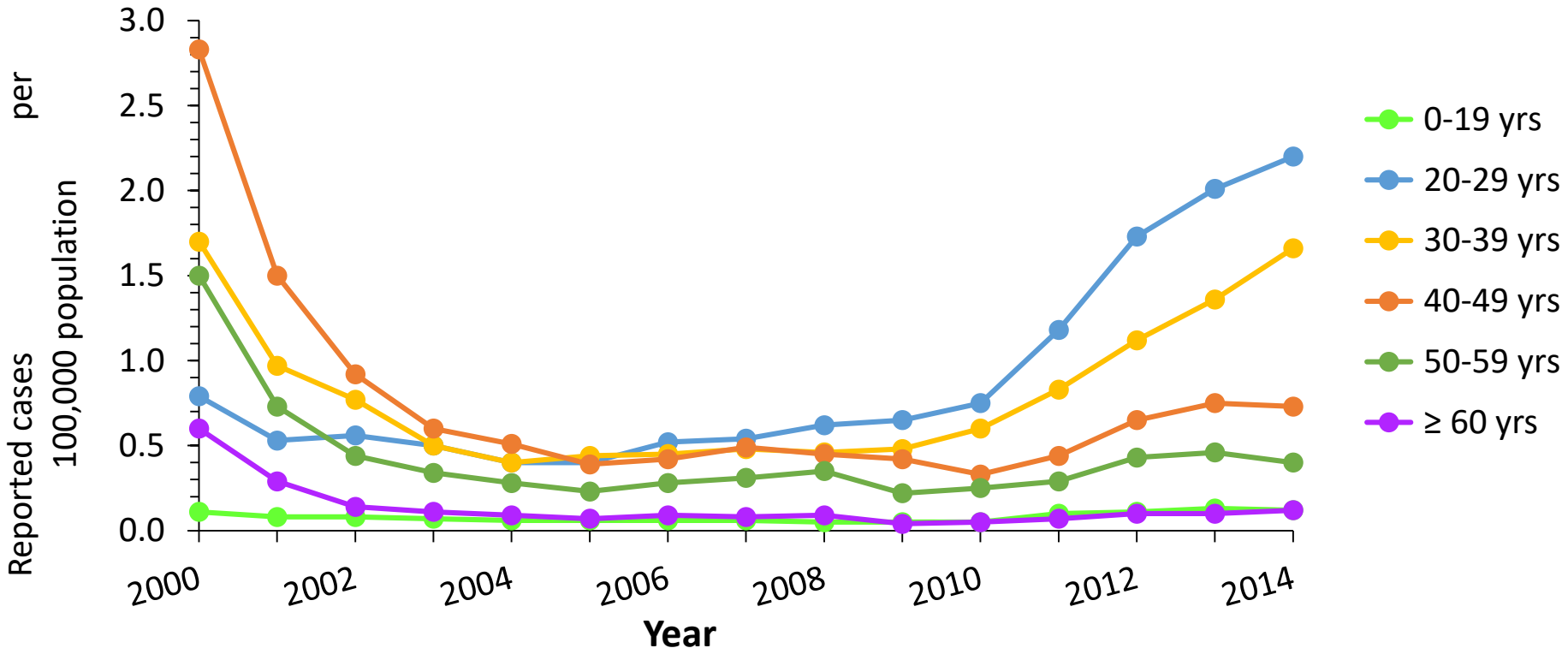


Zibbell J, 2015 MMWR, 64(17): 444-448

Incidence of Acute Hepatitis C, By Age Group — United States National Notifiable Diseases Surveillance System, 2000-2014



CDC National Viral Hepatitis Surveillance System data

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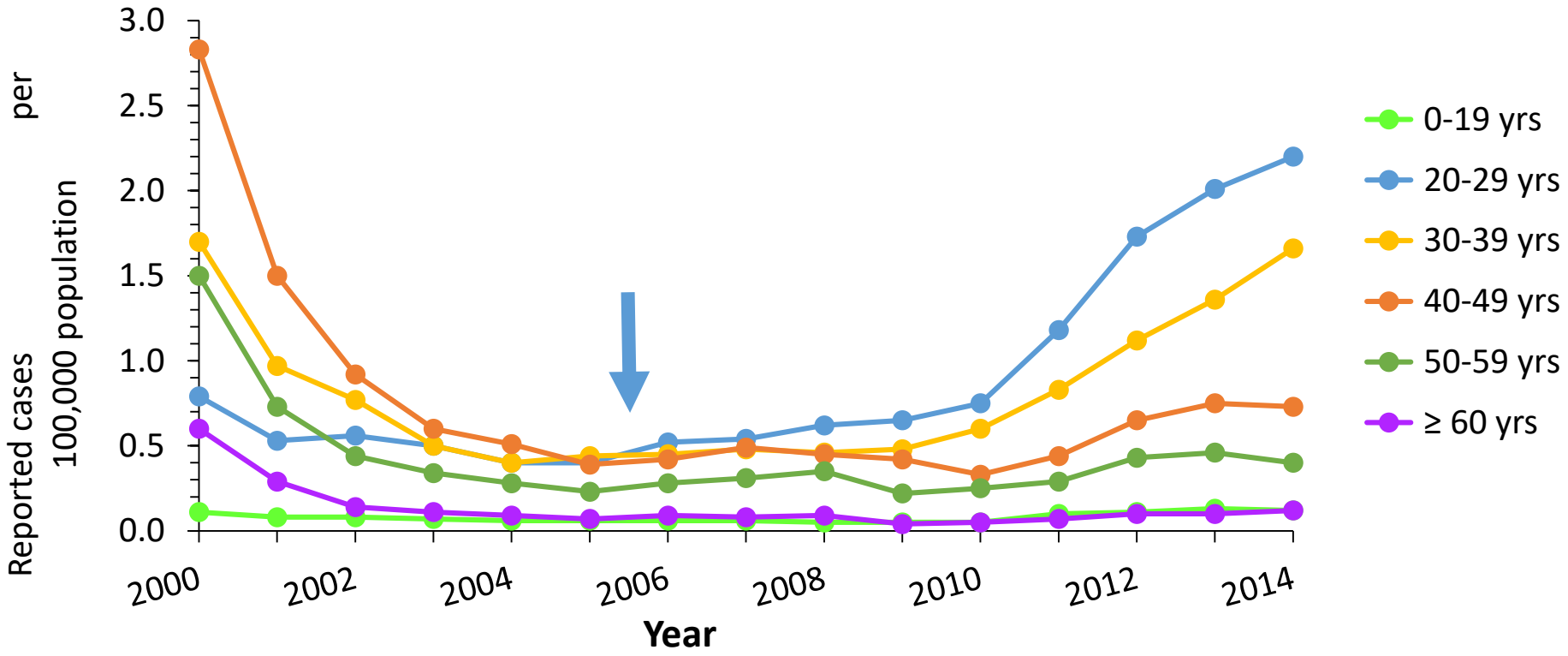

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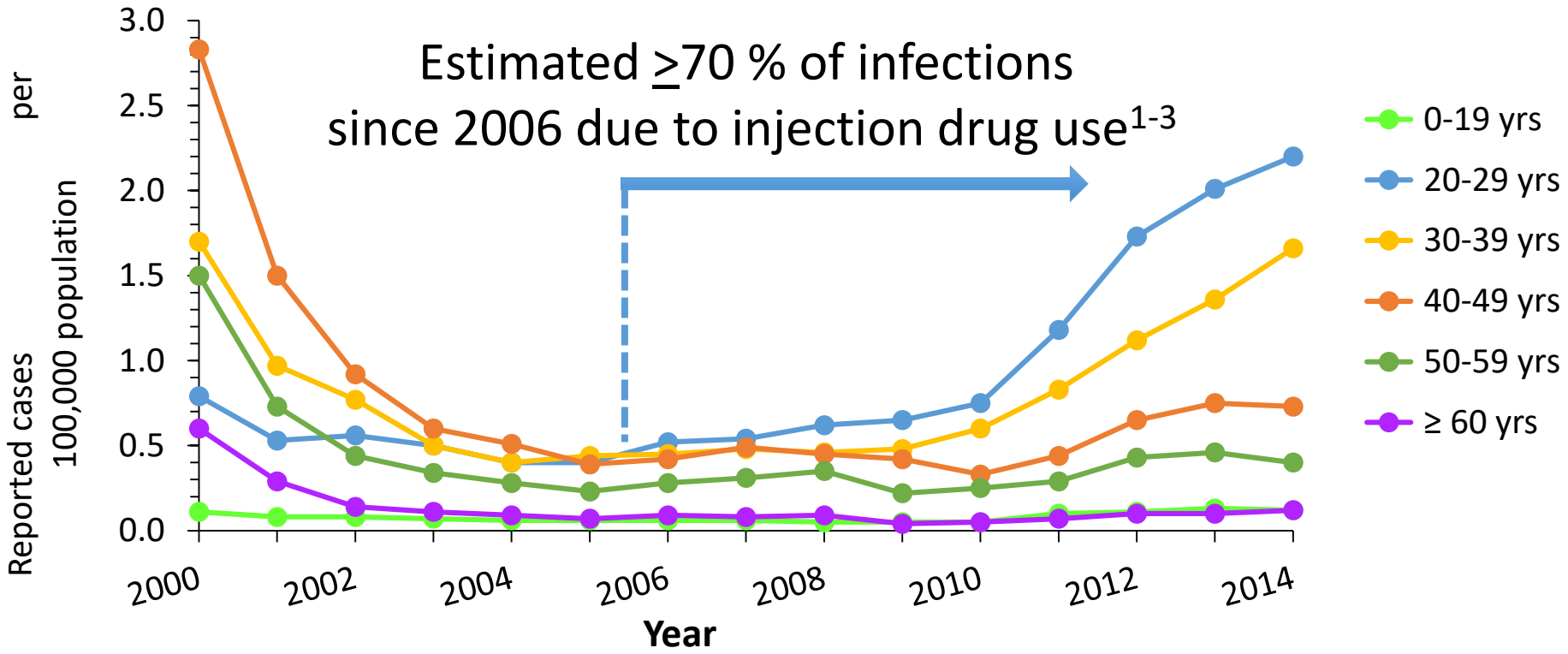

1. Zibbell, 2015, MMWR; 64(17): 453-8. 2. Suryaprasad, 2014, Clin Infect Dis; 59(10):1411-9. 3.
3. CDC, 2014; Viral hepatitis surveillance -- United States, 2013.

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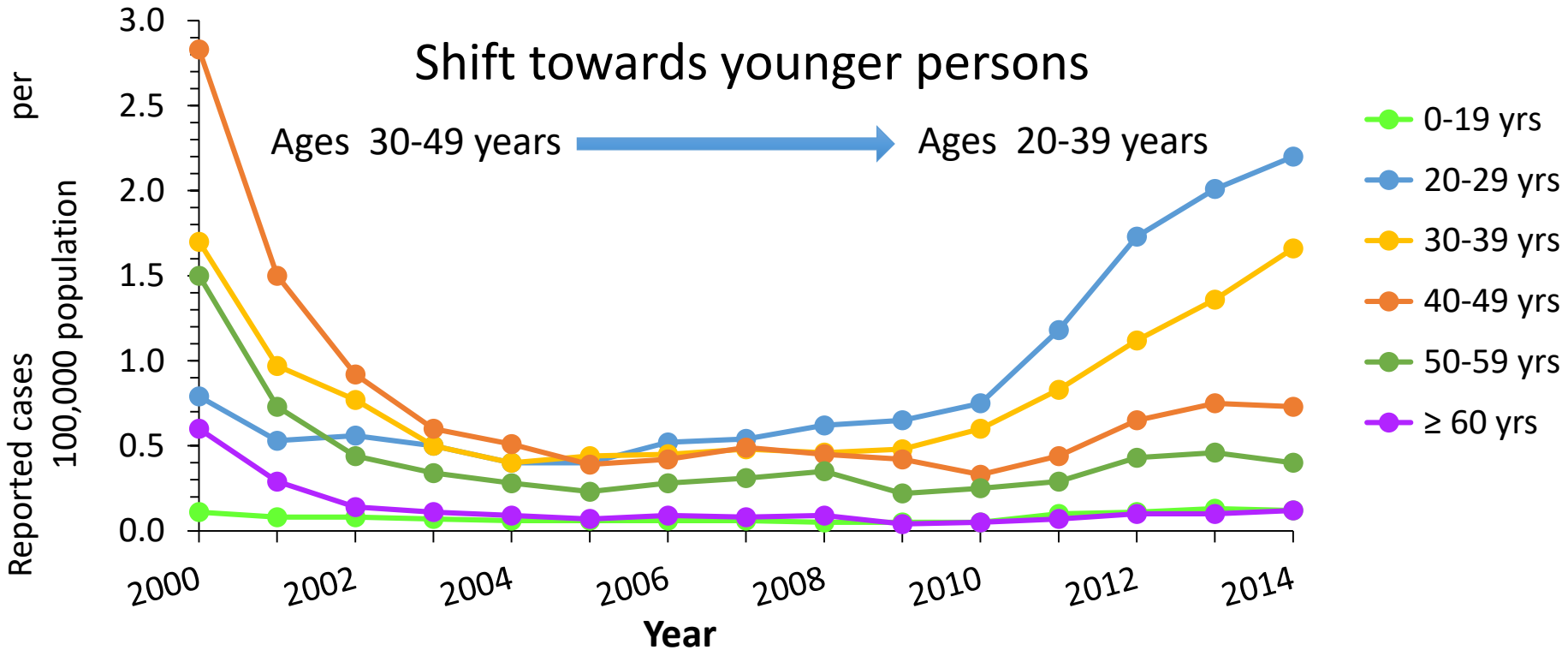


How Else is the Demography of Injection Drug Use Changing Based on PWID* Infected with HIV and Acute HCV?

Demographic	Traditionally….	Increasingly….
Geographic focus	Urban	Rural and Semi-urban
Race/ethnicity	Black and Latino/Hispanic	White
Male-to-female ratio	2:1	1:1

* persons who inject drugs

Where Could an Event like Scott County Happen Next?

CDC assessed which U.S. counties are potentially vulnerable to rapid dissemination of HIV/HCV infection among persons who inject drugs (i.e., an event like that which occurred in Scott County?)

Methods: Multi-step Approach

Which variables best predict injection drug use?

- **Poisson Regression Model**
  - → used acute HCV infection as proxy outcome for IDU
  - → factors known or plausibly associated with IDU
  - → had to be national-level data, recent, complete

Which counties have highest vulnerability to HCV/HIV outbreak?

- **Composite Index Score – "Vulnerability Score"**
  - → added weighted values of predictor variables for each county to create a sum vulnerability score
  - → rank ordered high-to-low by vulnerability score

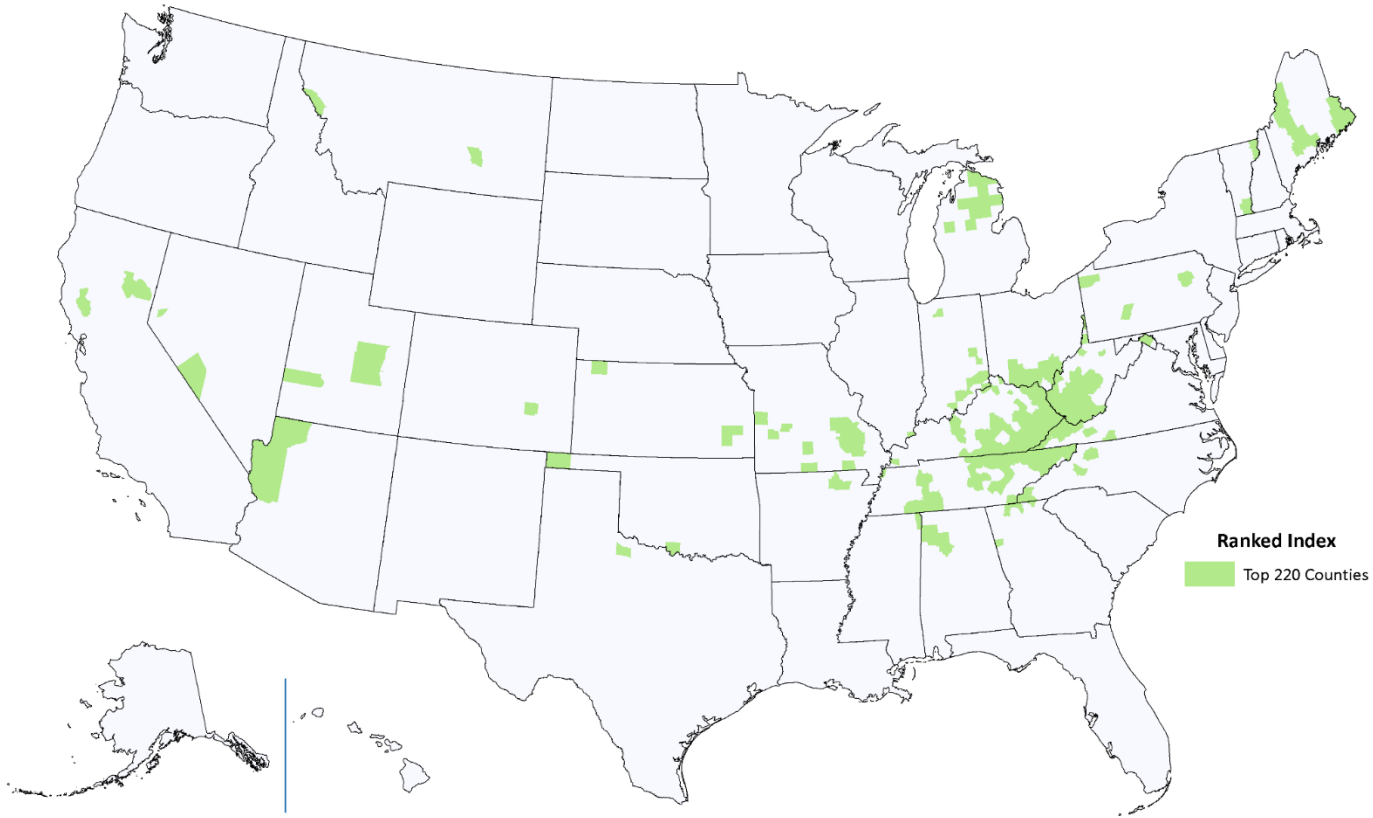
Results: Which variables best predicted acute HCV infection?

Variables	Final Model	
	Standardized Relative Risk	p-value
Percent White, Non-Hispanic Population[1]	1.68	<0.0001
Drug Overdose Deaths per 100K Persons	1.21	<0.0001
Per Capita Income[2]	0.81	<0.0001
Percent Unemployed Population[3]	1.14	0.012
Prescription Opioid Sales per 10K persons[4]	1.09	0.013
Buprenorphine Prescribing Potential by Waiver per 10K Persons[5]	1.08	0.010

1. Percent of the county population of white, non-Hispanic race/ethnicity
2. Mean income computed for every person in the county; derived by dividing the total income of all people 15 years and older by the total population; modeled as log base 10
3. Percent of civilian persons aged 16 years and older unemployed and actively seeking work
4. Rate of morphine milligram equivalent kilograms sold of opioid pain relievers per 10,000 population
5. Evidence of need for addiction services

van Handel, 2016, JAIDS, 73(3): 323-31

Counties Highly Vulnerable to New HIV or Viral Hepatitis Infections Due to Unsafe Injection Drug Use



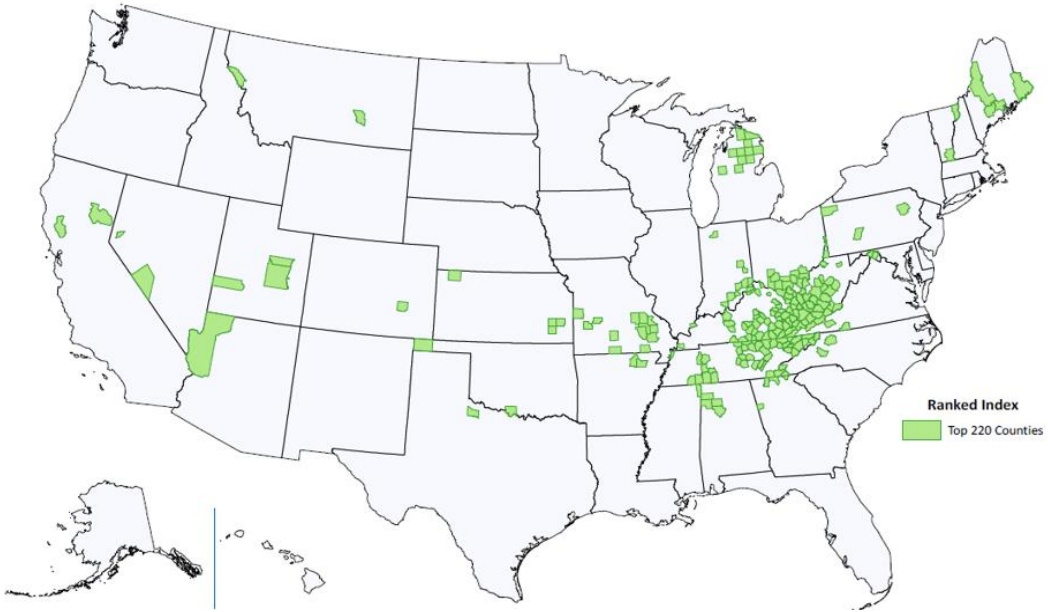
van Handel, 2016, JAIDS, 73(3): 323-31

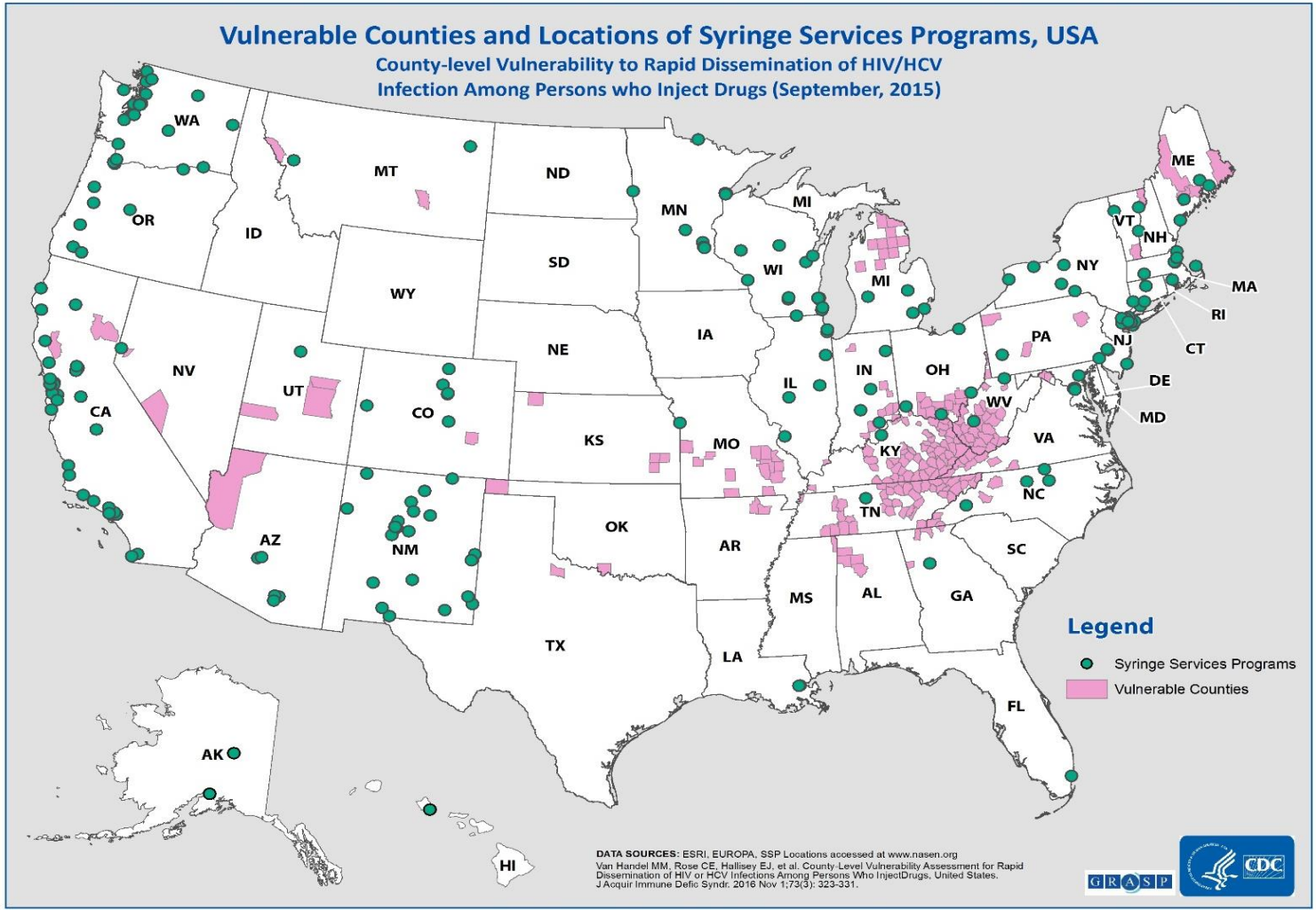
Identified potential indicators of injection drug use

Tested association with proxy of active injection drug use (e.g., acute HCV infections)

Derived parsimonious set of predictor indicators

Used indicators to identify most vulnerable counties

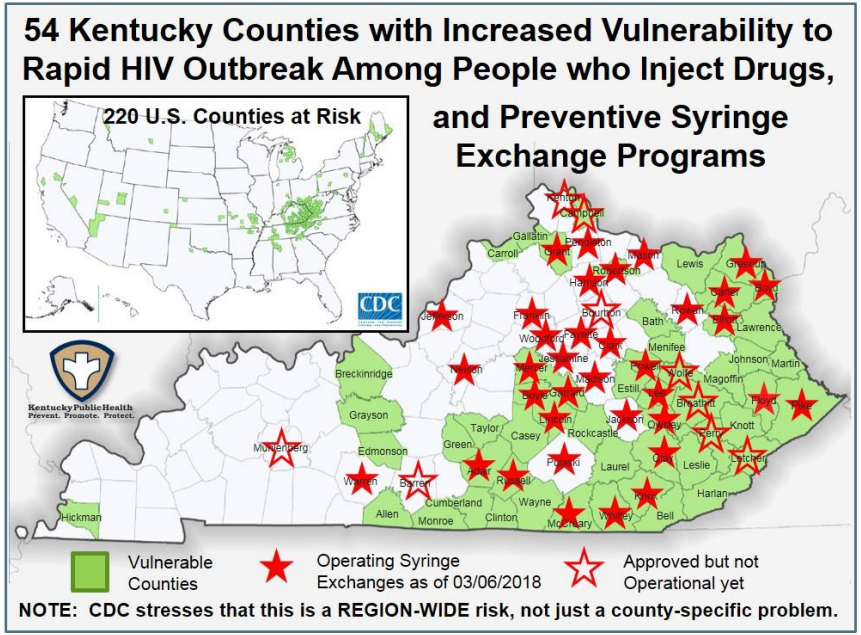



Vulnerable Counties and Locations of Syringe Services Programs, USA
County-level Vulnerability to Rapid Dissemination of HIV/HCV Infection Among Persons who Inject Drugs (September, 2015)
WA
OR
CA
ID
NV
MT
WY
UT
AZ
CO
NM
ND
SD
NE
KS
OK
TX
MN
IA
MO
AR
LA
WI
IL
MS
MI
IN
KY
TN
AL
OH
WV
GA
FL
SC
NC
VA
PA
NY
ME
VT
NH
MA
RI
CT
NJ
DE
MD
AK
HI
Legend
Syringe Services Programs
Vulnerable Counties
DATA SOURCES: ESRI, EUROPA, SSP Locations accessed at www.nasen.org
Van Handel MM, Rose CE, Hallisey EJ, et al. County-Level Vulnerability Assessment for Rapid Dissemination of HIV or HCV Infections Among Persons Who Inject Drugs, United States. J Acquir Immune Defic Syndr. 2016 Nov 1;73(3): 323-331.
GRASP
CDC

Using Vulnerability Assessment to Inform Action

Spring 2016 = 15 SSPs

Spring 2018 = 54 SSPs



Encourage State-Based Evaluation: Novel Data Sources

Public Safety

- Drug overdose deaths (esp. opioids)
- Poison center calls for drug overdose
- Naloxone administrations
- Arrests for drug possession or sales
- Other drug-related crime

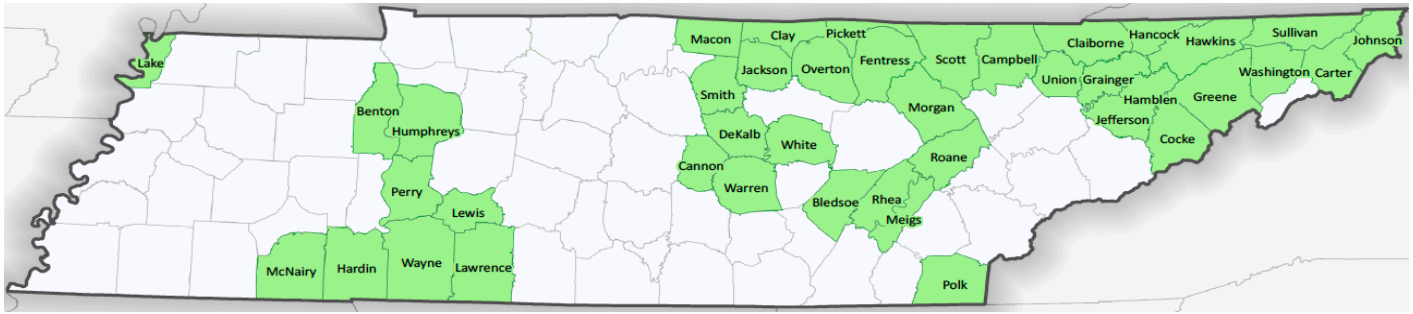
Healthcare Systems

- Treatment for drug overdose
- EMS calls for drug overdose
- Medical examiner toxicology record
- Bacterial infections related to IDU
- Prescription drug monitoring program

Substance Use Disorder Services

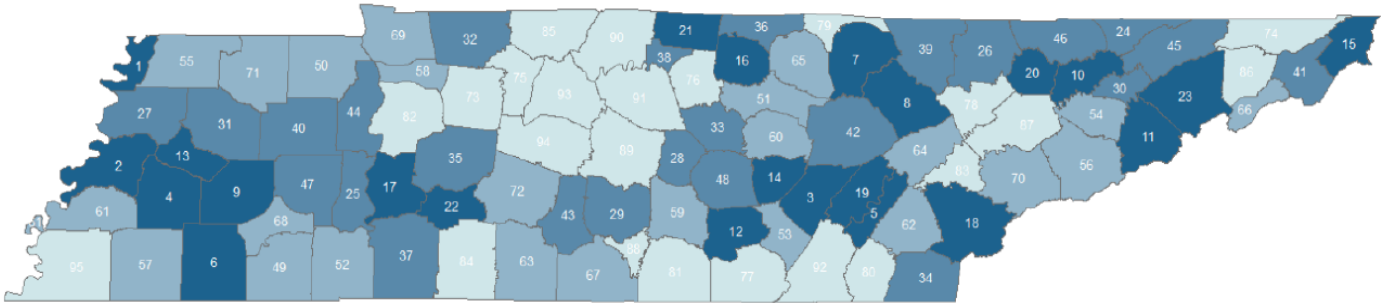
- Admissions to rehabilitation centers
- Administration of medication-assisted therapy (e.g., methadone, buprenorphine, naltrexone)

Tennessee's In-State Vulnerability Assessment



Variables from PDMP refined TN assessment

- Opioid/heroin ODs
- Morphine milligram equivalent (MME) prescribing

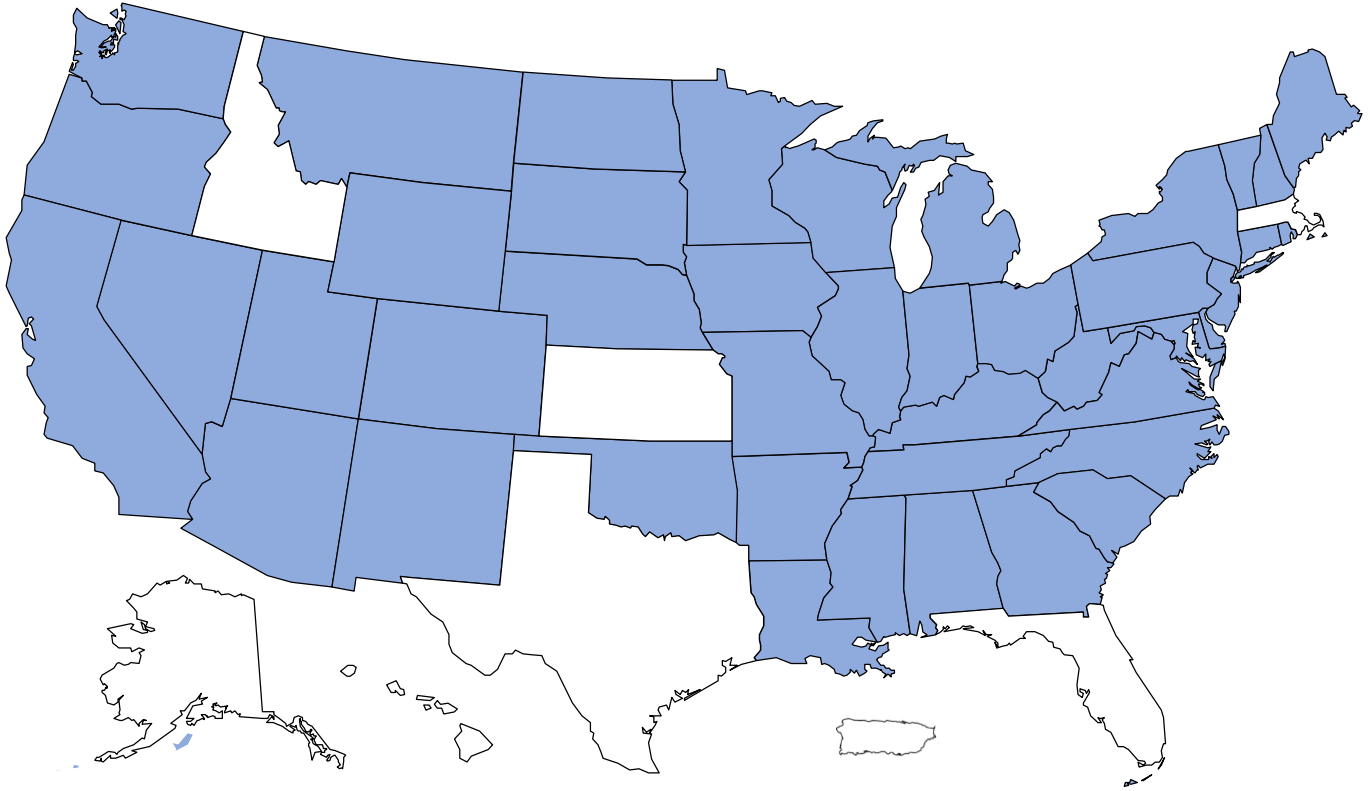


Vulnerability Rank

- Ranks 1-24, More Vulnerable
- Ranks 25-48
- Ranks 49-72
- Ranks 73-95, Less Vulnerable

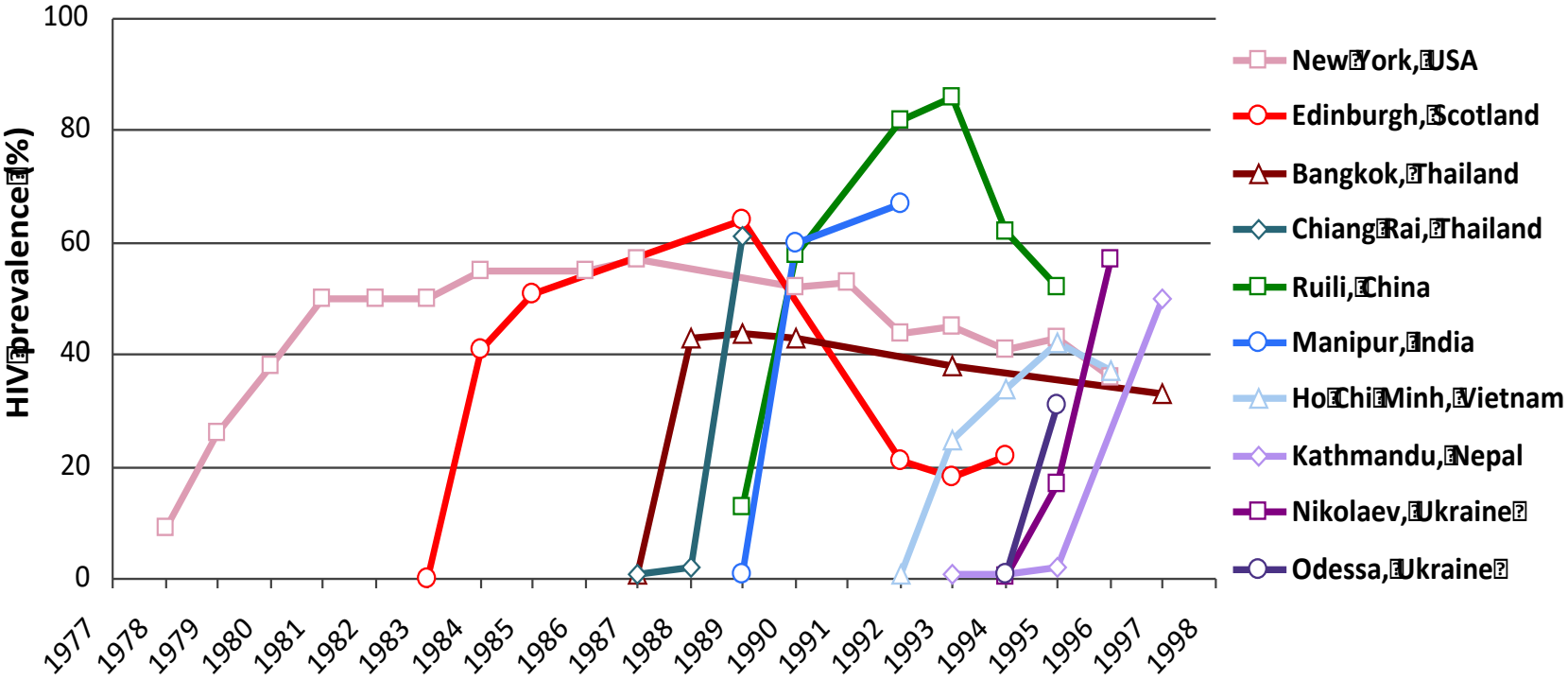
Source: Michael Rickles, et al.;Tennessee's In-State Vulnerability Assessment for a 'Rapid Dissemination of HIV or HCV Infection' Event Utilizing Data about the Opioid Epidemic, Clinical Infectious Diseases, , cix1079, https://doi.org/10.1093/cid/cix1079

States Assessing Local Vulnerability to HIV/HCV Outbreaks Among Persons Who Inject Drugs, 2019



Explosive Increases in HIV Prevalence among PWID, 1978-1998

40% and higher prevalence may be reached within 1-2 years



UN Reference Group on HIV/AIDS Prevention and Care among IDU in Developing and Transitional Countries, www.idurefgroup.org, Courtesy of Richard Needle

Effective Treatment Prevents Sexual HIV Transmission

HPTN 052	→	1,763 heterosexual mixed HIV-status couples
PARTNER 1 & 2	→	888 heterosexual mixed HIV-status couples 972 male homosexual mixed HIV-status couples
OPPOSITES ATTRACT	→	358 male homosexual mixed HIV-status couples

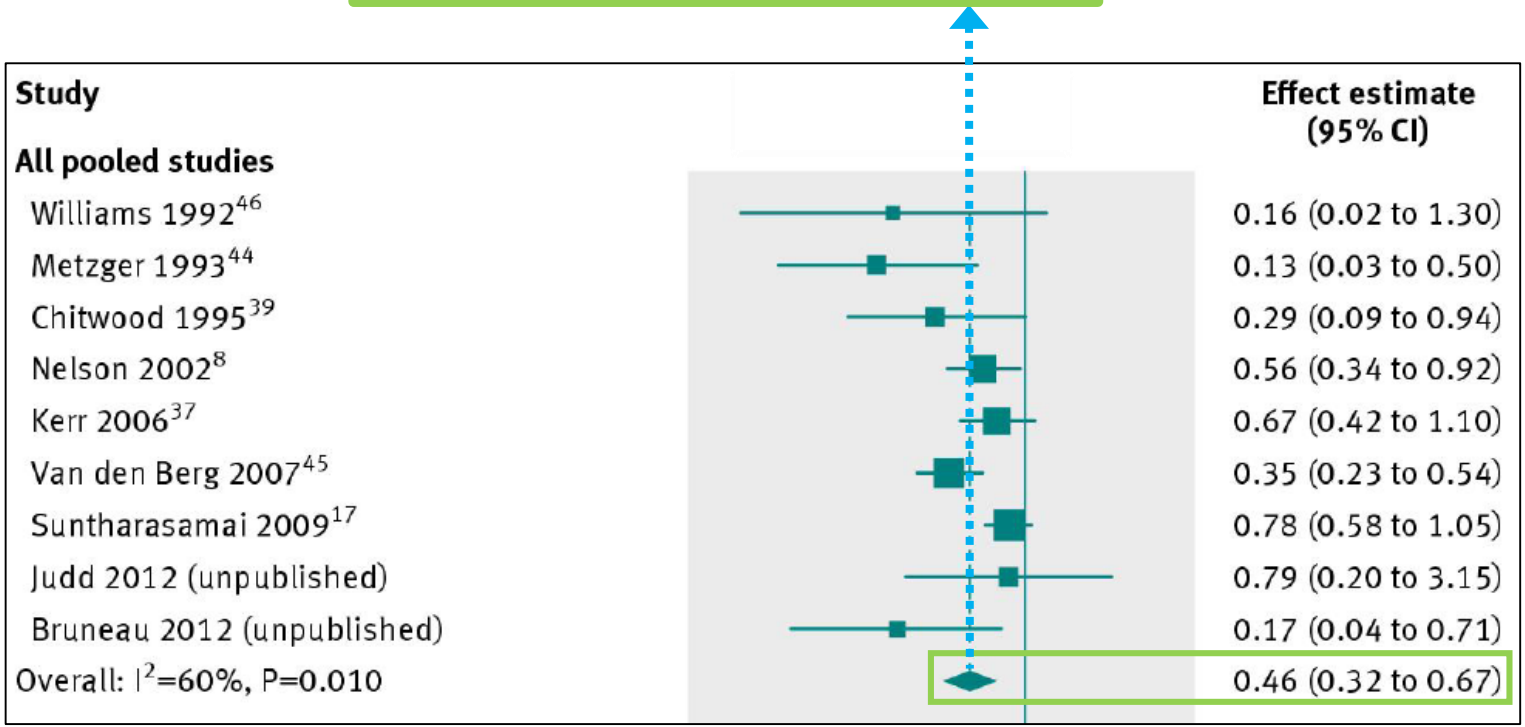
144,631 condomless acts of vaginal and anal intercourse (P1&2, OA)
over > 1,500 couple years of observation
No phylogenetically linked transmissions observed

- Effectiveness to prevent HIV transmission by other routes not studied
- Expect it would be very high and possibly comparable

Source: Cohen et al., N Engl J Med 2016, 375(9):830-839, Rodger et al., JAMA 2016, 316(2):171-181, Bavinton et al., Lancet 2018, published ahead of print
Rodger et al. Lancet 2019, published ahead of print

Opioid Substitution Therapy Reduces HIV Transmission

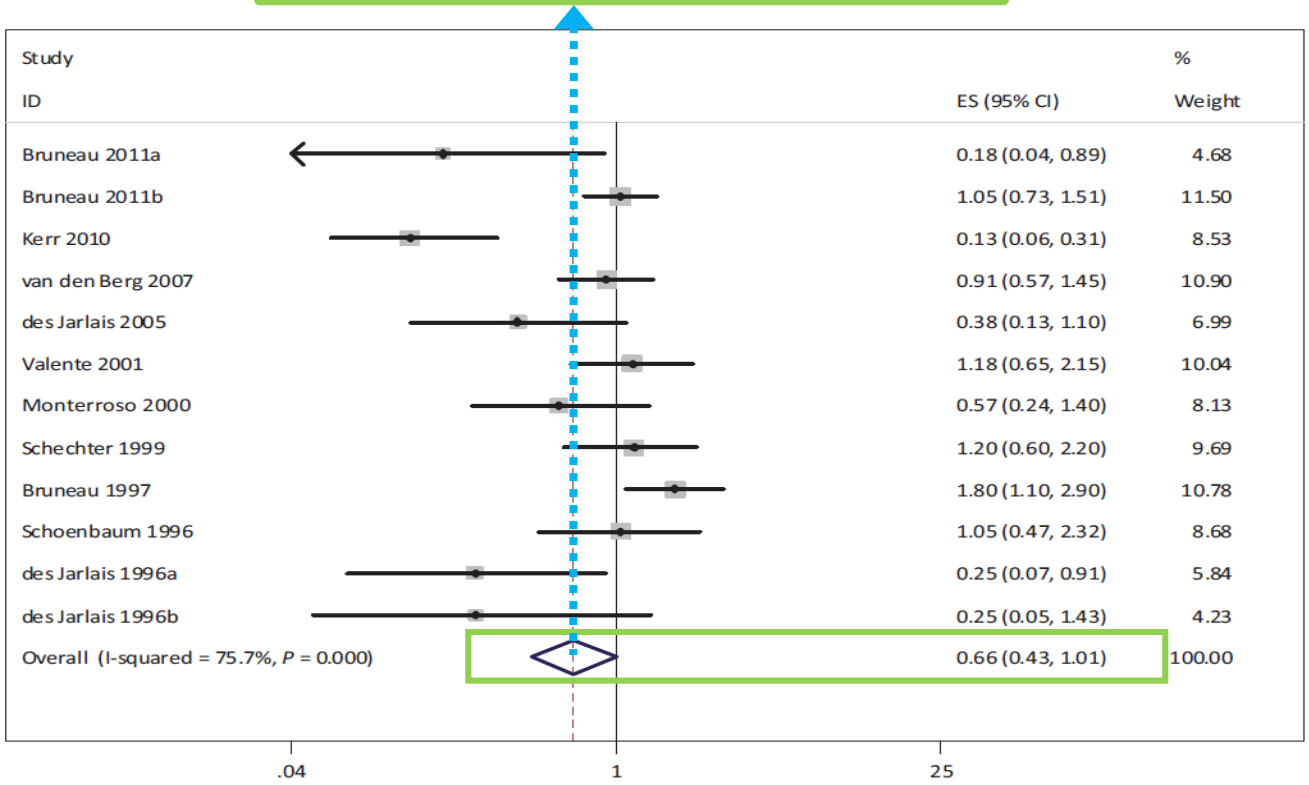
64% reduction in risk of HIV infection



MacArthur G J et al., BMJ 2012, Courtesy of Richard Needle

Needle and Syringe Programs Reduce HIV Incidence

56% reduction in risk of HIV infection

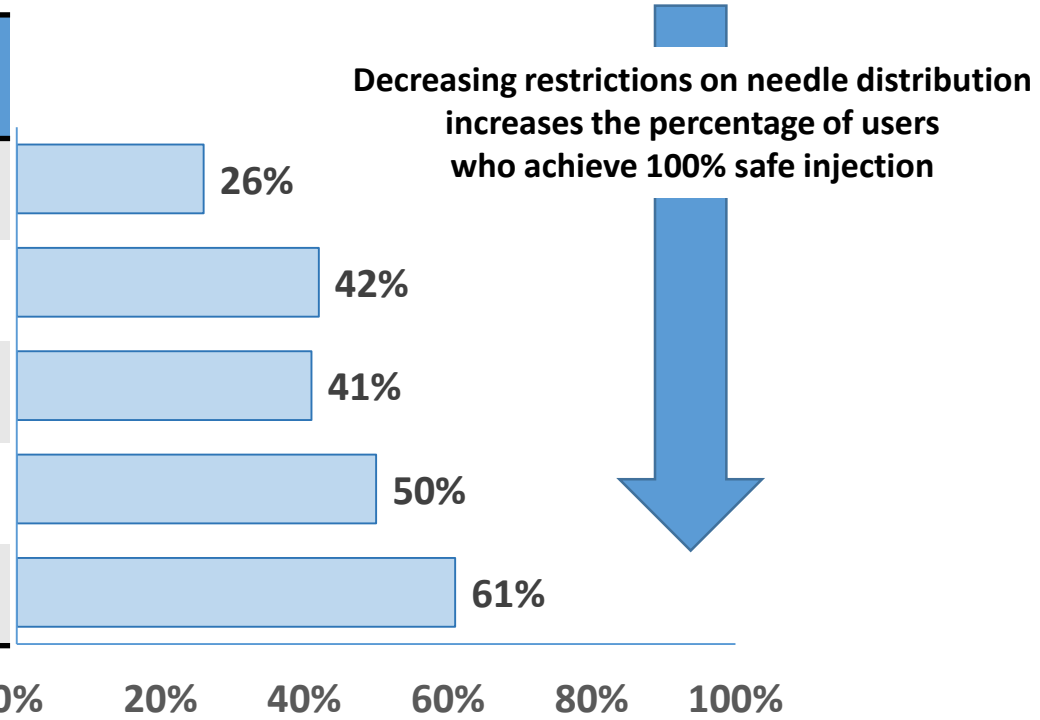


Aspinall E J et al., Int J Epidemiol 2014, Courtesy of Richard Needle

Restrictive SSP policies increase risk of infections

Percentage of clients achieving 100% injections with clean needles by distribution policy

Limit per visit*	1-to-1 only	No extra for emergency
X	X	X
	X	X
X	X	
	X	



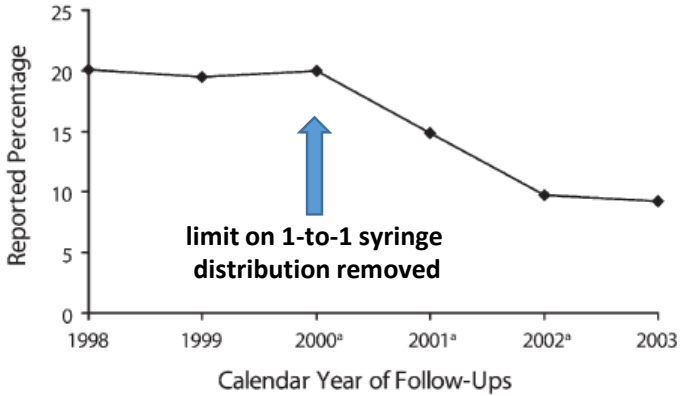
Blumenthal, 2007; Addiction, 102:638-646

* SSP imposed a per-visit cap on the total number of needles and syringes distributed

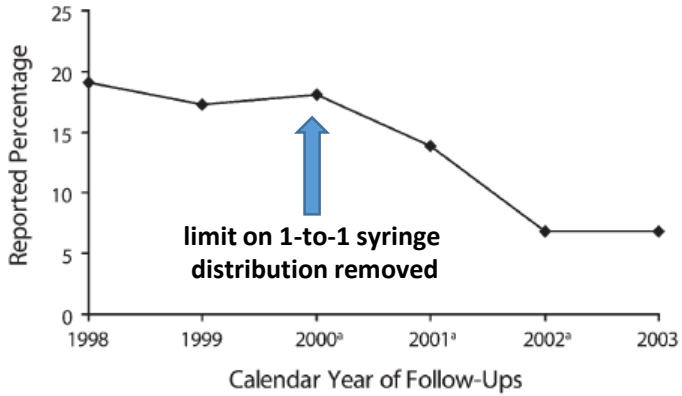
Removing “1-to-1” exchange policy reduces infection risks

Vancouver Injection Drug Users Study, Vancouver, British Columbia, 1998-2003

Syringe borrowing



Syringe lending

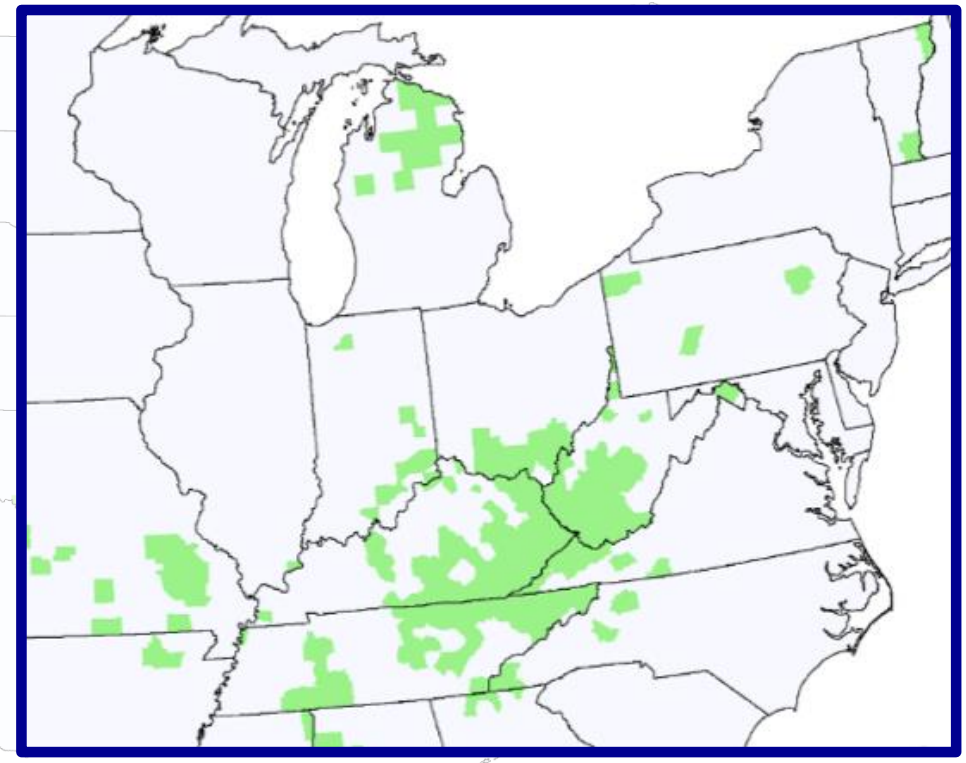


Kerr et al., Am J Pub Health 2010, 100(8):1449-1453

Counties Highly Vulnerable to New HIV or Viral Hepatitis Infections Due to Unsafe Injection Drug Use

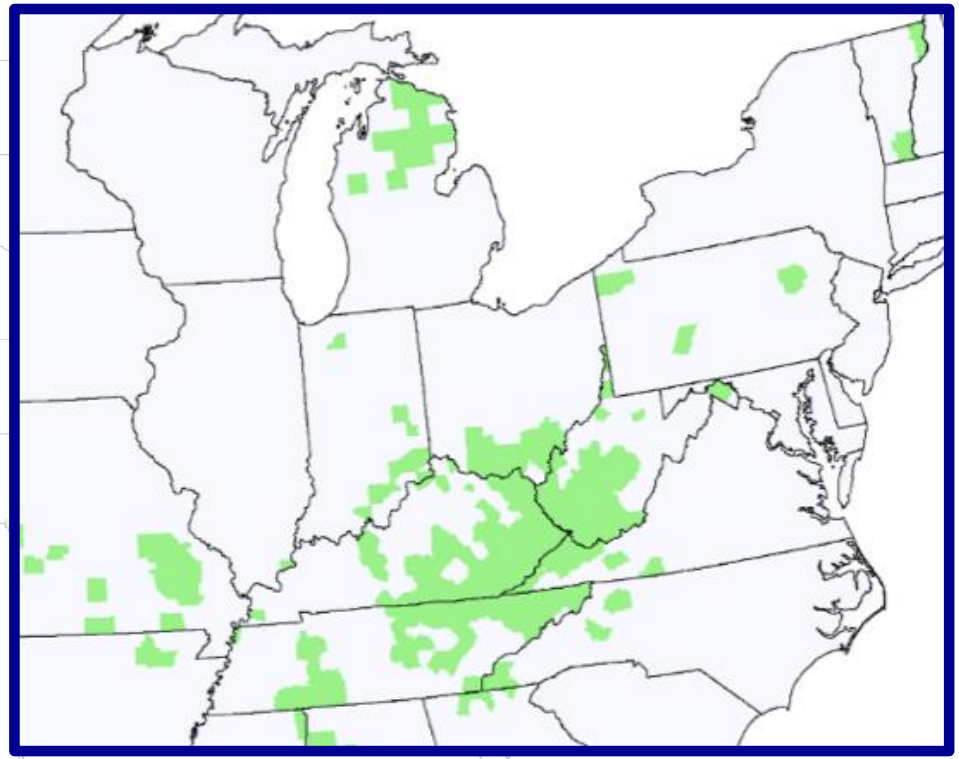
What do most of these counties share in common?

Predominately RURAL



Key challenging characteristics in rural areas (among others…)

1. Limited access to services
   - Large distances
   - Few transportation options
   - Uninsured
2. Distrust between PWID and law and community leaders
3. Limited infrastructure
   - HIV and viral hepatitis testing
   - Clinical HIV/HCV care services
   - Medication-assisted therapy
   - Syringe service programs



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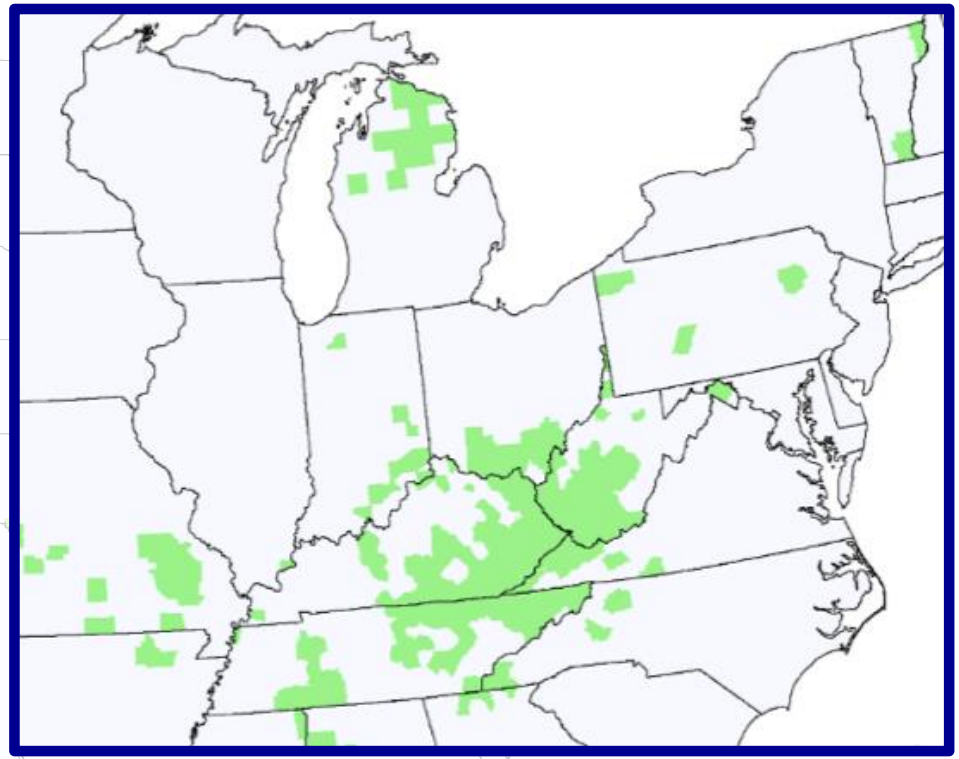


Engaging Law Enforcement, North Carolina Example

FAST FACTS ON SYRINGE EXCHANGE PROGRAMS

NC taxpayers paid $50 million for Hep C treatment and $117 million for HIV treatment in 2014 alone

Crime decreases in areas with a SEP because participants are connected to housing, food pantries and other social services

There is available funding from private foundations to cover the costs of a SEP. NC taxpayers won't have to foot the bill.

SEPs are a gateway to drug treatment. SEP participants are 5 times more likely to enter treatment than non-participants

SEPs prevent the spread of HIV, HCV and HBV, reducing the taxpayer burden for these diseases. A sterile syringe could prevent these diseases for 7 cents

SEPs collect discarded needles and dispose of them safely, thereby reducing the number of syringes in public areas

SEPs reduce needle-stick injury to law enforcement by 66%

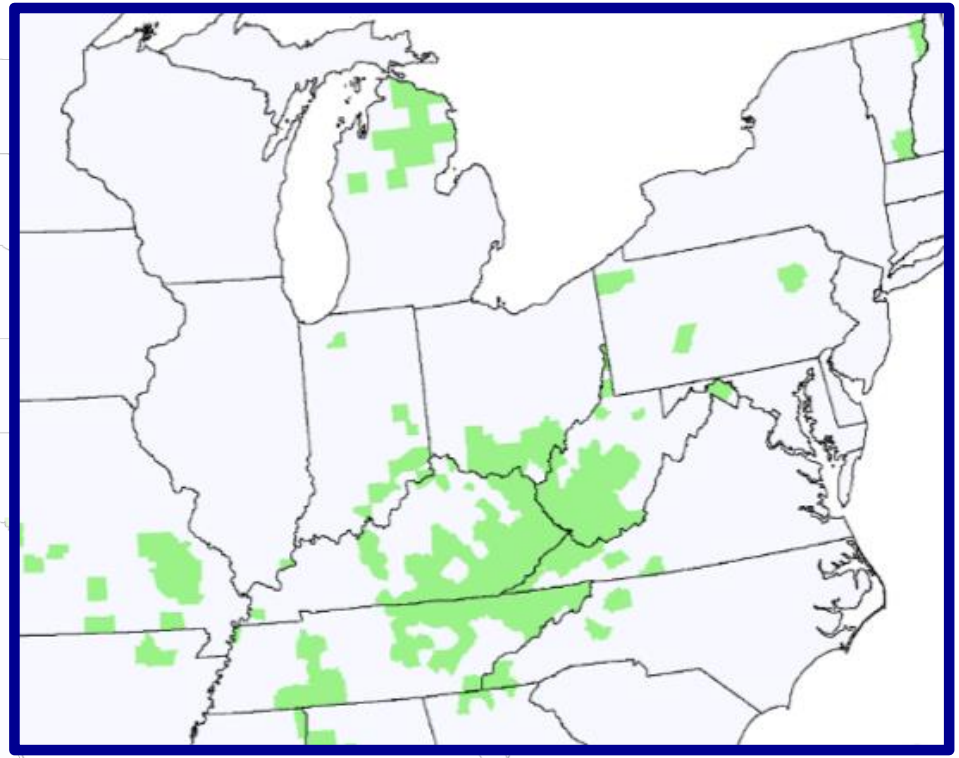
SEPs decrease hepatitis C transmission among people who inject drugs by as much as 50%. HIV injection rates have decreased by as much as 80% in areas with SEPs

For more information, visit www.nchrc.org

NORTH CAROLINA IN SOLIDARITY HARM REDUCTION COALITION

Key challenging characteristics in rural areas (among others…)

1. Limited access to services
   - Large distances
   - Few transportation options
   - Uninsured
2. Distrust between PWID and law and community leaders
3. Limited infrastructure
   - HIV and viral hepatitis testing
   - Clinical HIV/HCV care services
   - Medication-assisted therapy
   - Syringe service programs



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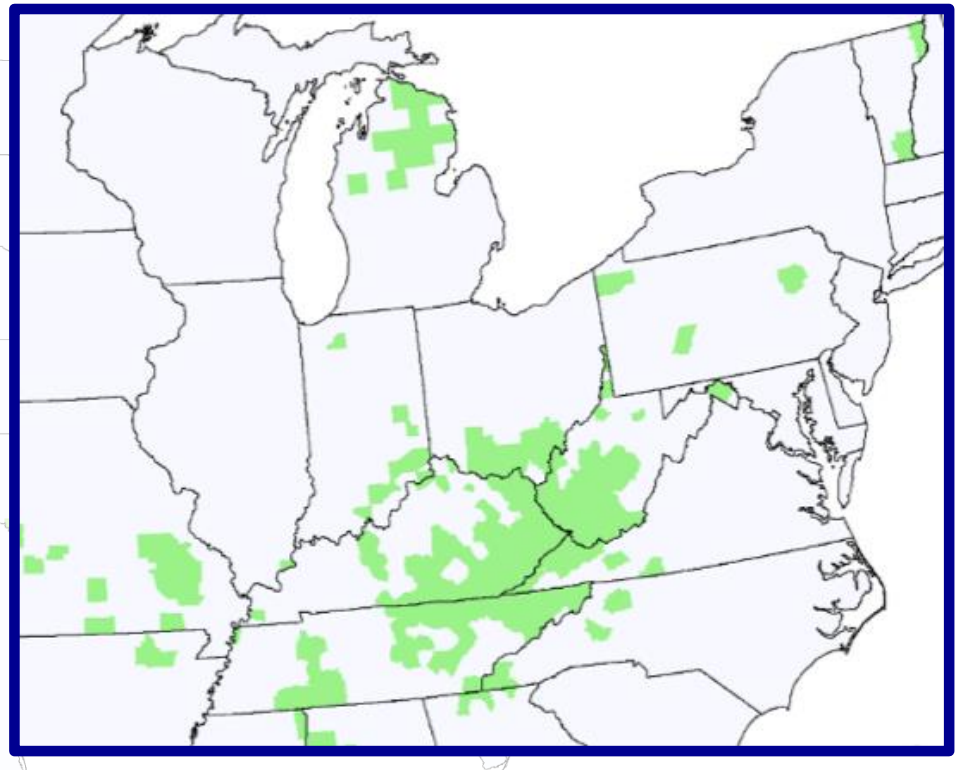
may also be illegal



Indiana Emergency Declaration and New Law Permitted Syringe Exchange in Response to Outbreak

After Temporary Emergency Actions, Indiana Passes Law to Allow Syringe Exchange Programs

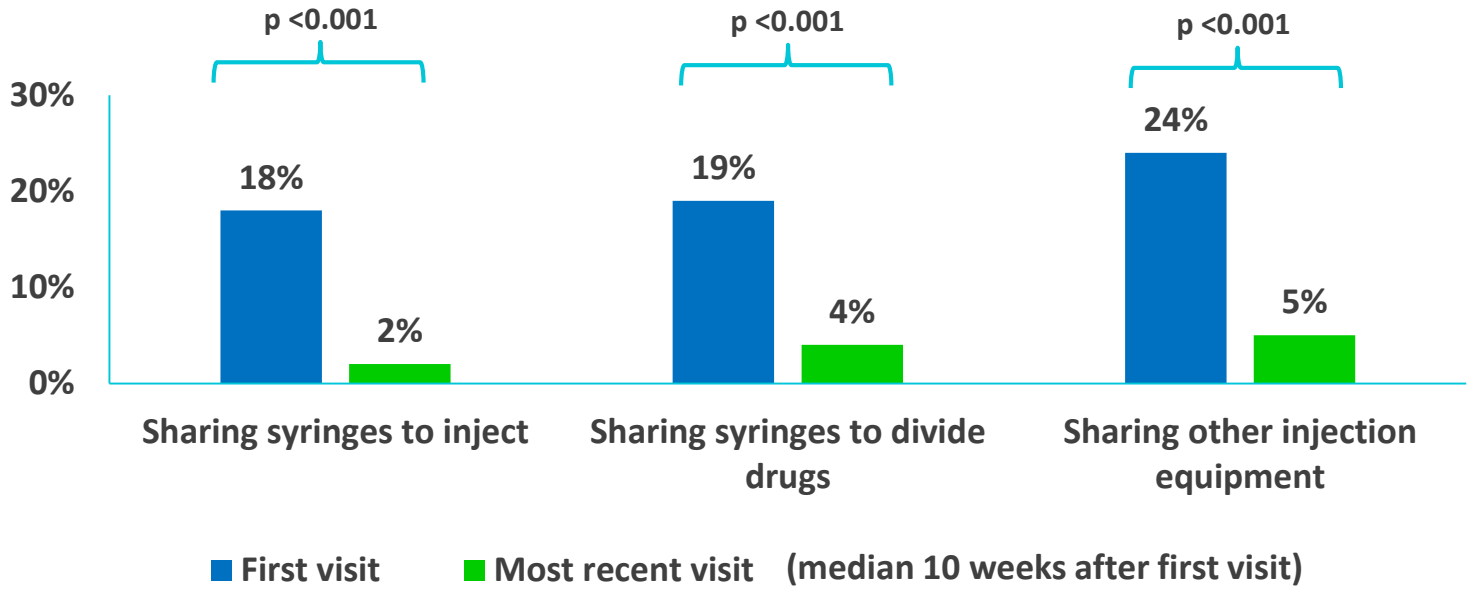
*From AIDS United

Indiana Governor Mike Pence has signed a bill approved by the state legislature this week giving local officials across the state the ability to create syringe exchange programs if they are experiencing a disease outbreak tied to injection drug use. The signed bill, Senate Enrolled Bill 461, is part of a broader response to the recent outbreak of HIV infections in the southeastern part of the state, which was initially caught surprised and ill-equipped for HIV prevention or response.

http://ohioaidscoalition.org/wp-content/uploads/OAC-Policy-Update-5_8_15.pdf

Impact of Syringe Exchange in Scott County

- **Reductions in sharing syringes and injection equipment (n=148)**



Patel *et al.* IDWeek 2015, abstract: J Acquir Immune Defic Syndr 2018; 77(4): 373-382.

Prosecutor urges against needle exchange

Keith Roysdon , kroysdon@muncie.gannett.com 12:14 p.m. ET April 25, 2017

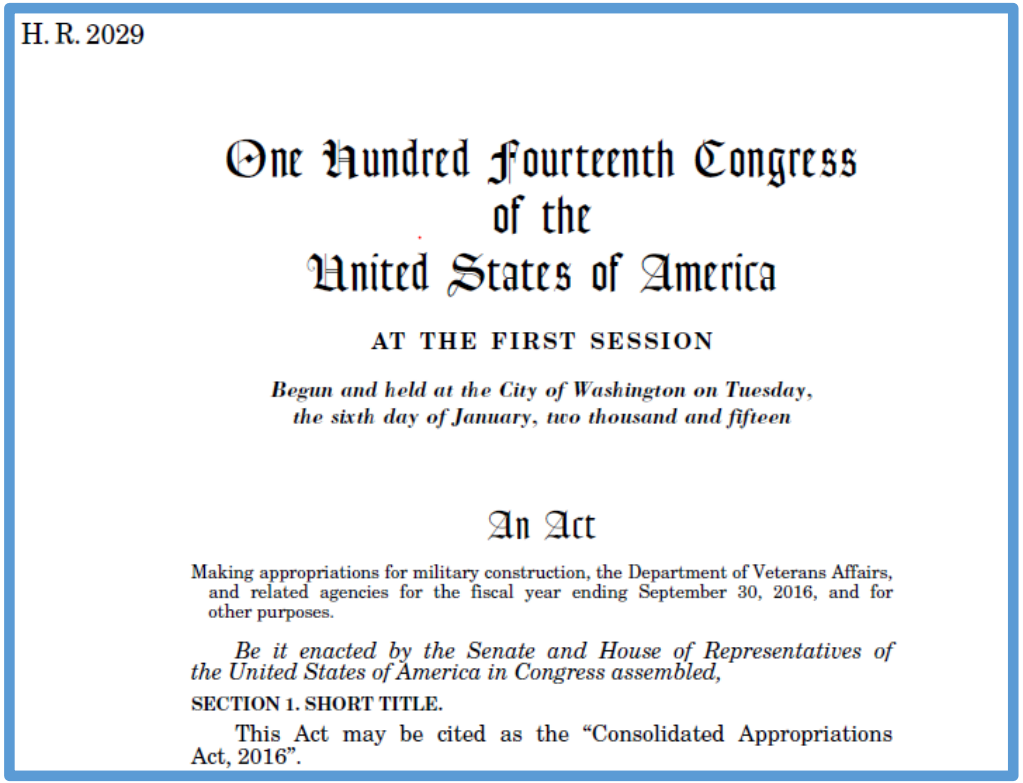
A needle exchange kit as displayed by Delaware County Prosecutor Jeffrey Arnold.
(Photo: Keith Roysdon / The Star Press)

Buy Photo

Arnold showed members of Delaware County Council in their meeting Tuesday morning a bag of supplies distributed in neighboring Madison County. Contents of the needle exchange kit included hundreds of fresh needles, condoms, saline for use in injections, small heroin "cookers" with twist-tie handles and a bio-hazard container for used needles, which Arnold said was the only positive item in the bags.

"This is enabling," Arnold told council members about the kits. "There are only two things missing: heroin and a lighter."

2016 Consolidated Appropriations Act: Federal Funds Can Now be Used to Support SSPs



H. R. 2029

One Hundred Fourteenth Congress
of the
United States of America

AT THE FIRST SESSION

Begun and held at the City of Washington on Tuesday, the sixth day of January, two thousand and fifteen

An Act

Making appropriations for military construction, the Department of Veterans Affairs, and related agencies for the fiscal year ending September 30, 2016, and for other purposes.

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled,

SECTION 1. SHORT TITLE.

This Act may be cited as the "Consolidated Appropriations Act, 2016".

2016 Consolidated Appropriations Act: Federal Funds Can Now be Used to Support SSPs

- Still prohibits use of federal funds for sterile needles or syringes
- Allows for federal funds to be used for other components of SSPs but first **health department must demonstrate need for SSPs in consultation with CDC:**

Jurisdiction is…

- ***experiencing***

or

- ***at risk for***

…significant increase in…

- ***hepatitis infections***

or

- ***HIV outbreak***

…due to

- ***injection drug use***

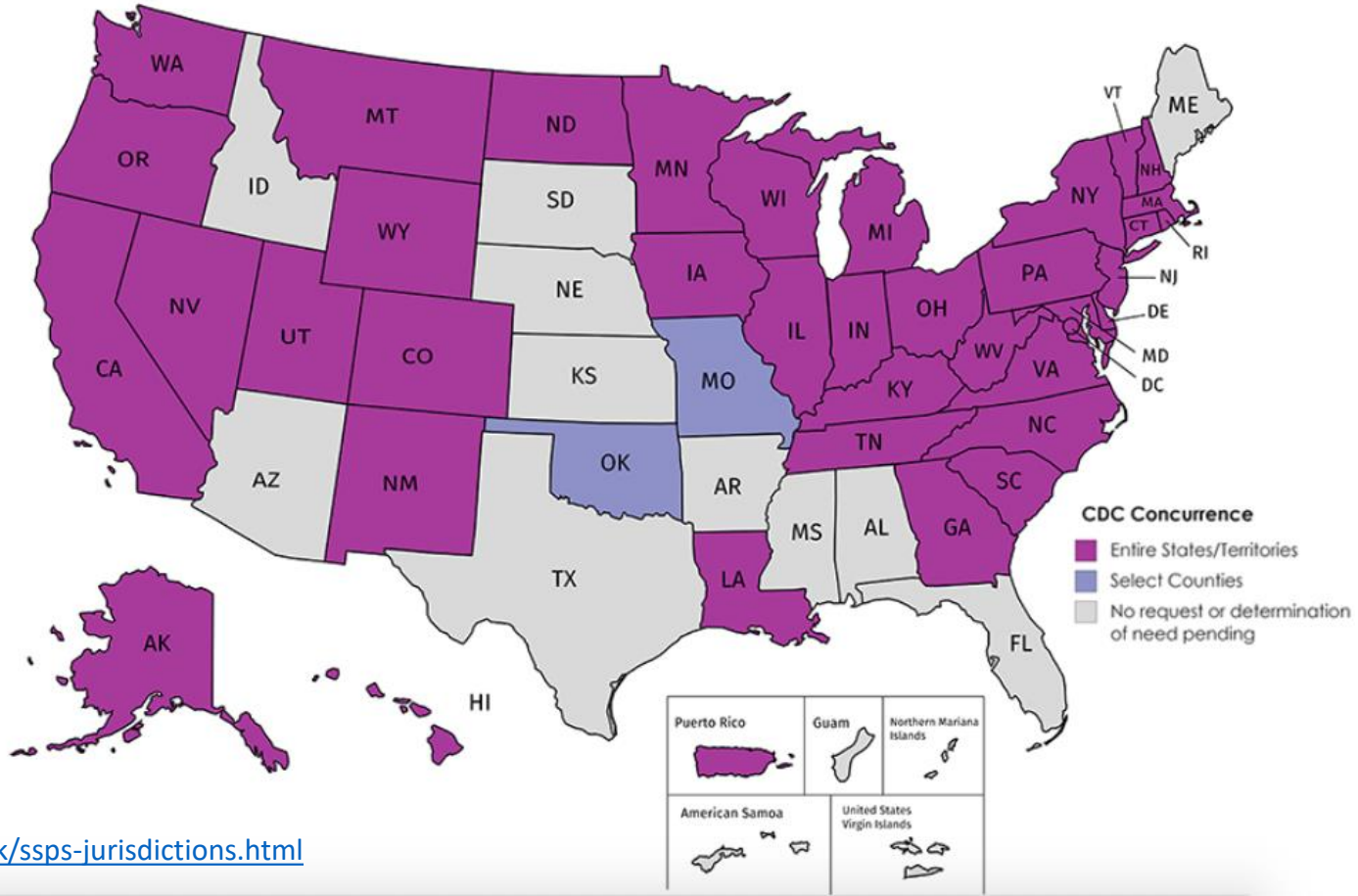
2016 Consolidated Appropriations Act: Federal Funds Can Now be Used to Support SSPs

- Any health department can apply
- Compiling the data required to demonstrate need creates a compelling narrative for action

http://www.cdc.gov/hiv/risk/ssps-jurisdictions.html

Determination of Need – CDC Concurrences as of June 2019

37 States and DC
1 Tribal nation
1 Territory
6 Counties
1 City



https://www.cdc.gov/hiv/risk/ssps-jurisdictions.html

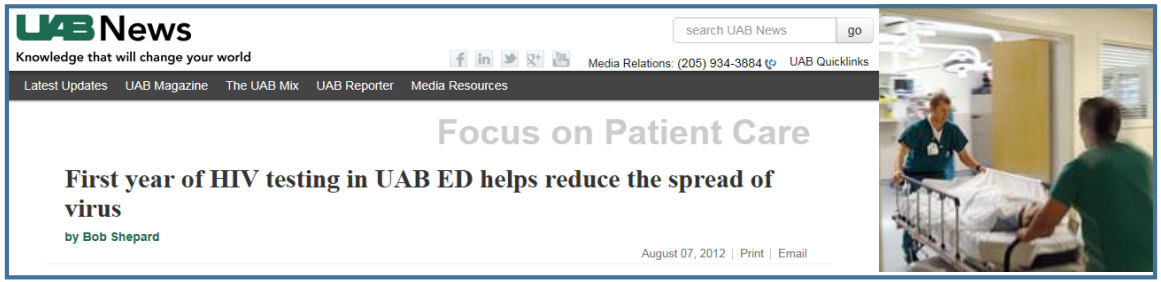
Recommendations for Local Public Health Departments to Detect, Prevent, and Respond to Outbreak

1. **Determine if unsafe injection of drugs is occurring**
   - Monitor data sources that may indicate injection drug use
   - Improve surveillance for acute HCV infection

Recommendations for Local Public Health Departments to Detect, Prevent, and Respond to Outbreak

2. Enhance testing for HIV and HCV infections

- Providers of services for persons with substance use disorder
- Jails and prisons
- Emergency departments and in-patient settings

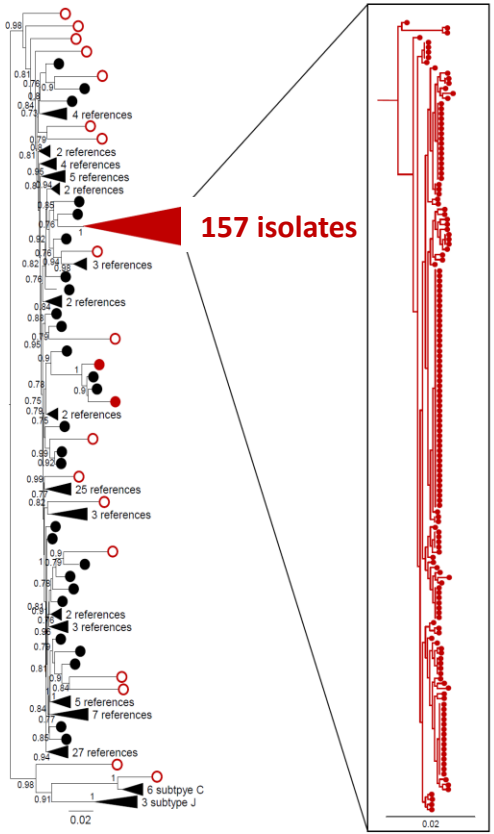


Recommendations for Local Public Health Departments to Detect, Prevent, and Respond to Outbreak

3. **Prepare an action plan for a potential HIV outbreak**
   - Know your HIV (and HCV) treatment landscapes
   - Draft a plan, engage emergency preparedness, run tabletop

Indiana 2015 HIV Outbreak
Laboratory Investigation of HIV Infections

Laboratory Investigation, 2015 Indiana HIV Outbreak
Phylogenetic Analysis of *pol* Sequences and Recency Testing*



SOURCE OF SAMPLE

- Indiana outbreak investigation
- Indiana reference sample (non-outbreak related)
- GenBank reference

- Single strain of HIV-1
- Mean nucleotide identity 99.7% (1302 base pairs)
- No antiretroviral drug resistance detected
- All infections epidemiologically linked to Scott County
- Availability of near real-time *pol* sequencing confirmed limited geographic spread of outbreak
- 85% of infections recent (limited in time)

Peters P. et al., N Engl J Med 2016;375(3):229-39

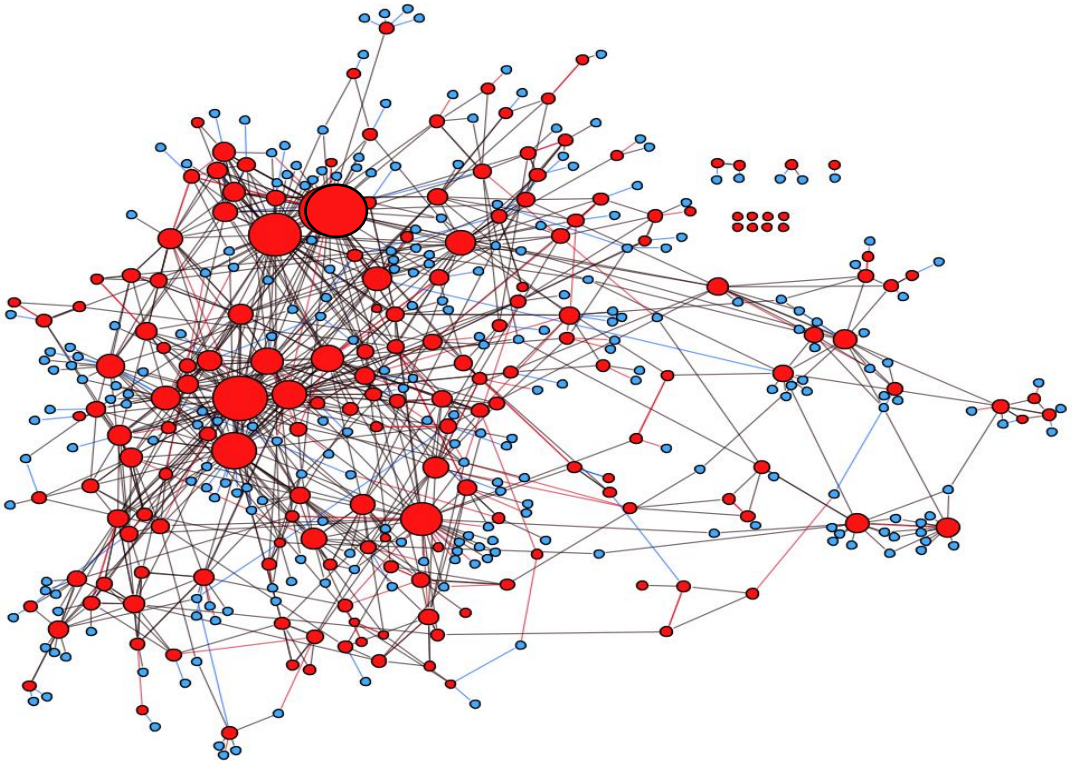
* Recency testing was performed using a Modified BioRad 1/2 Plus O Assay with avidity index cutoff set at 30%, corresponding to approximately 221 days

How did the infections spread?

Application of Computational Science for Cluster Analysis

1. Network of relationships and transmission risk behaviors
2. Genetic relatedness of infecting strains from each individual
3. Timing of infections

Infections Occurred in a Dense Network of PWID



Node Color

HIV +

HIV -

Edge Color

IDU

Sex and IDU

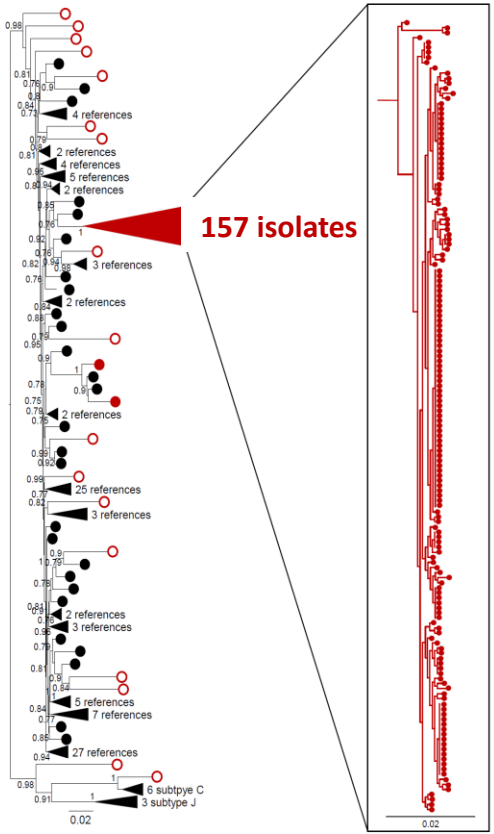
Sex

Size Scale

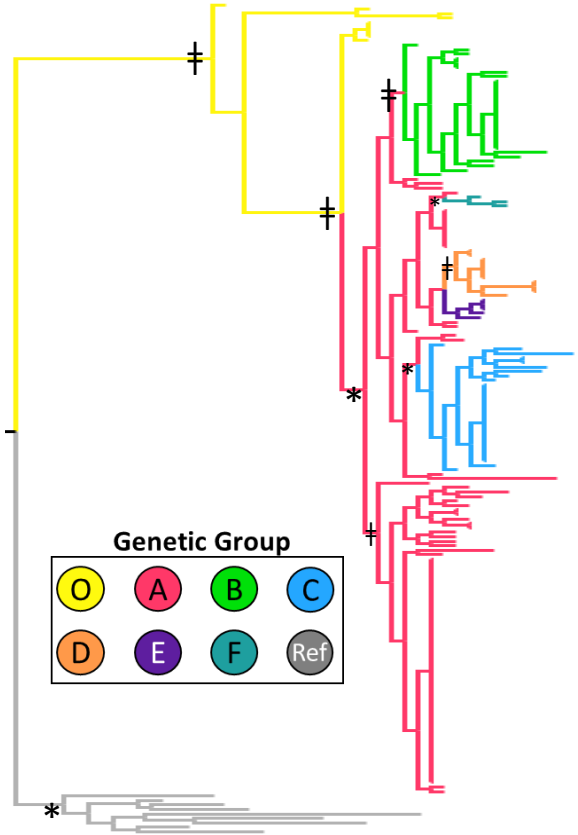
56 Total high risk contacts

Campbell E et al., J Infect Dis, 2017; 216(9):1053-1062

Transmission Cluster Investigation: Assess Genetic Distances

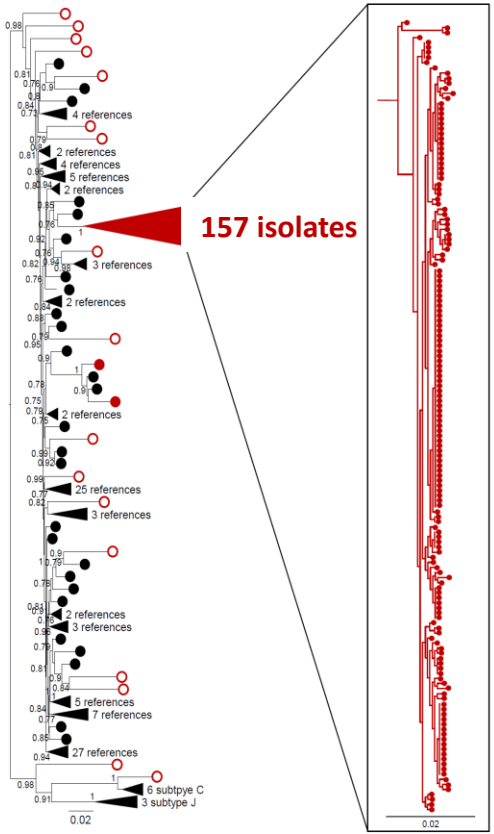


- Decreased genetic distance threshold from ≤ 1.5% to ≤ 0.1%
- 1-2 base substitution differences



Peters P. et al., N Engl J Med 2016;375(3):229-39; Campbell E et al., J Infect Dis, 2017; 216(9):1053-1062

Transmission Cluster Investigation: Create Genetic Network



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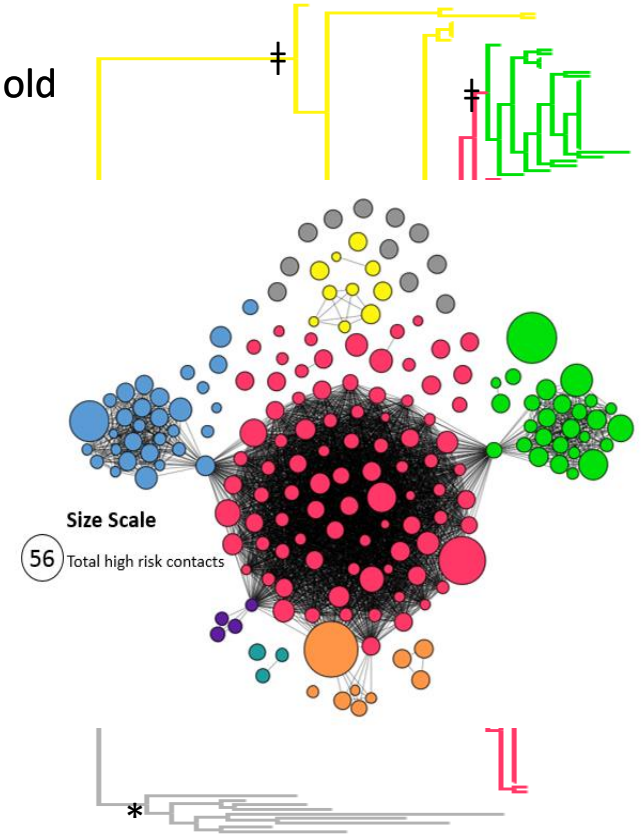

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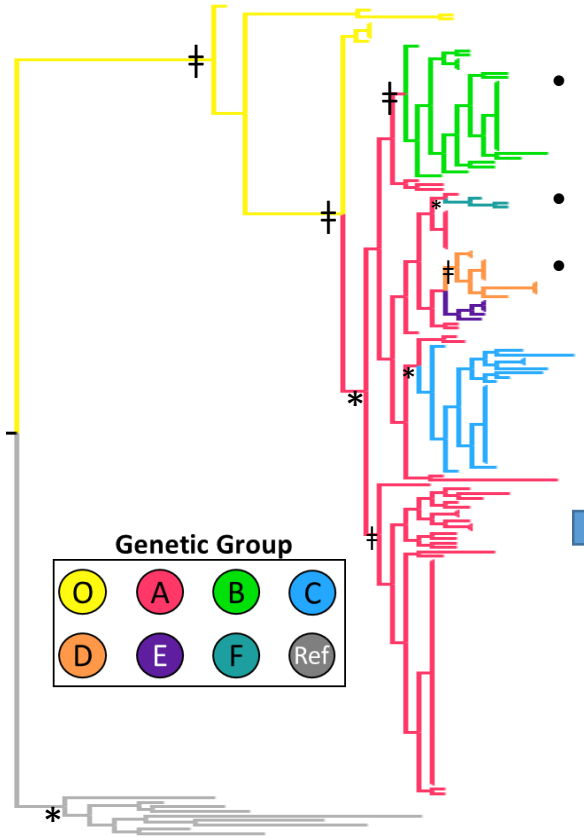
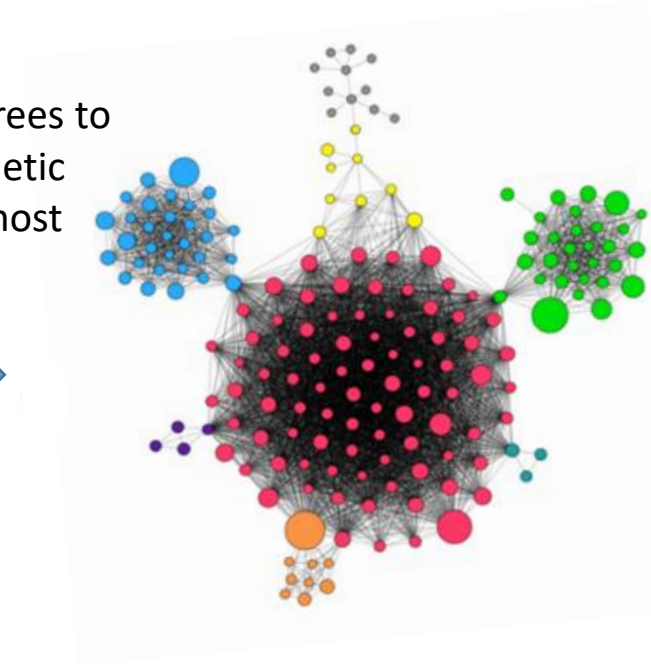


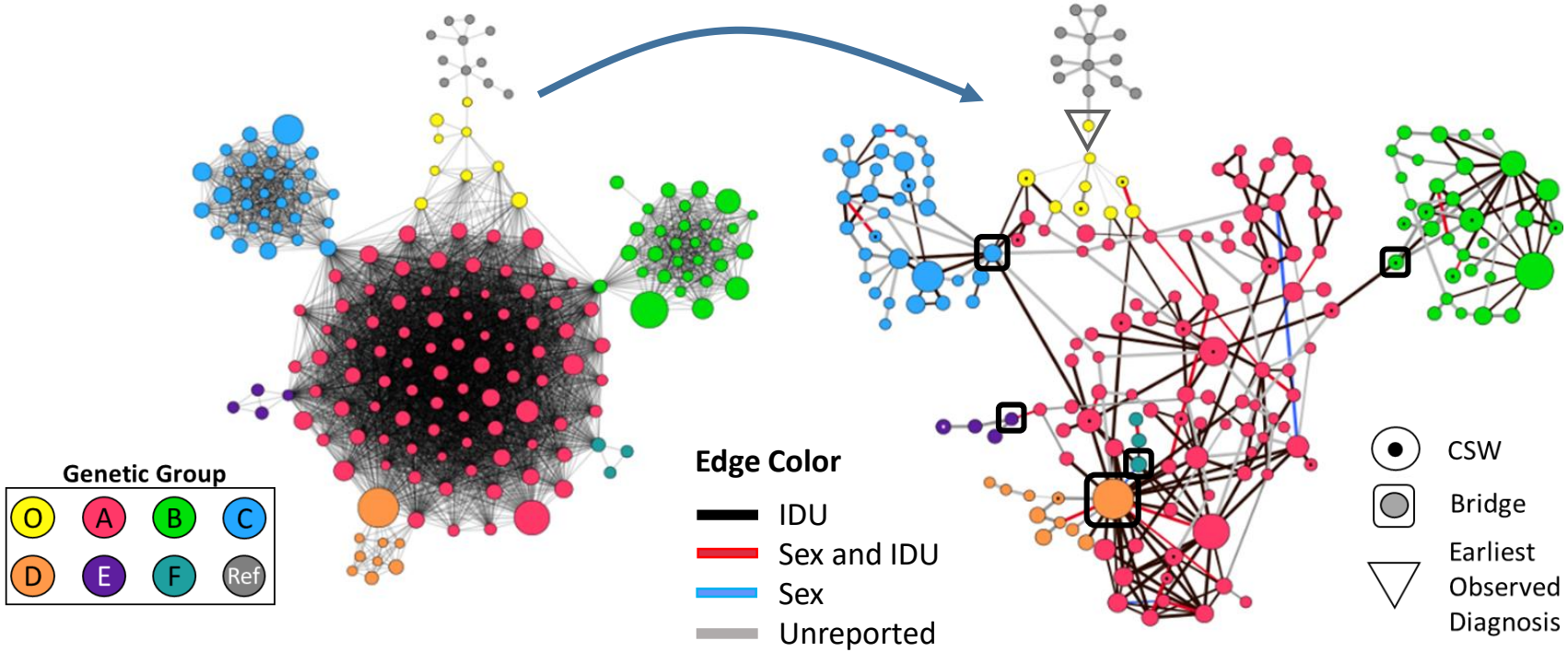
- Decreased genetic distance threshold from ≤ 1.5% to ≤ 0.1%
- 1-2 base substitution differences
- Constructed minimum spanning trees to find most parsimonious set of genetic distances required to create the most complete network possible



Campbell E. et al., J Infect Dis 2017; 216(9): 1053-1062

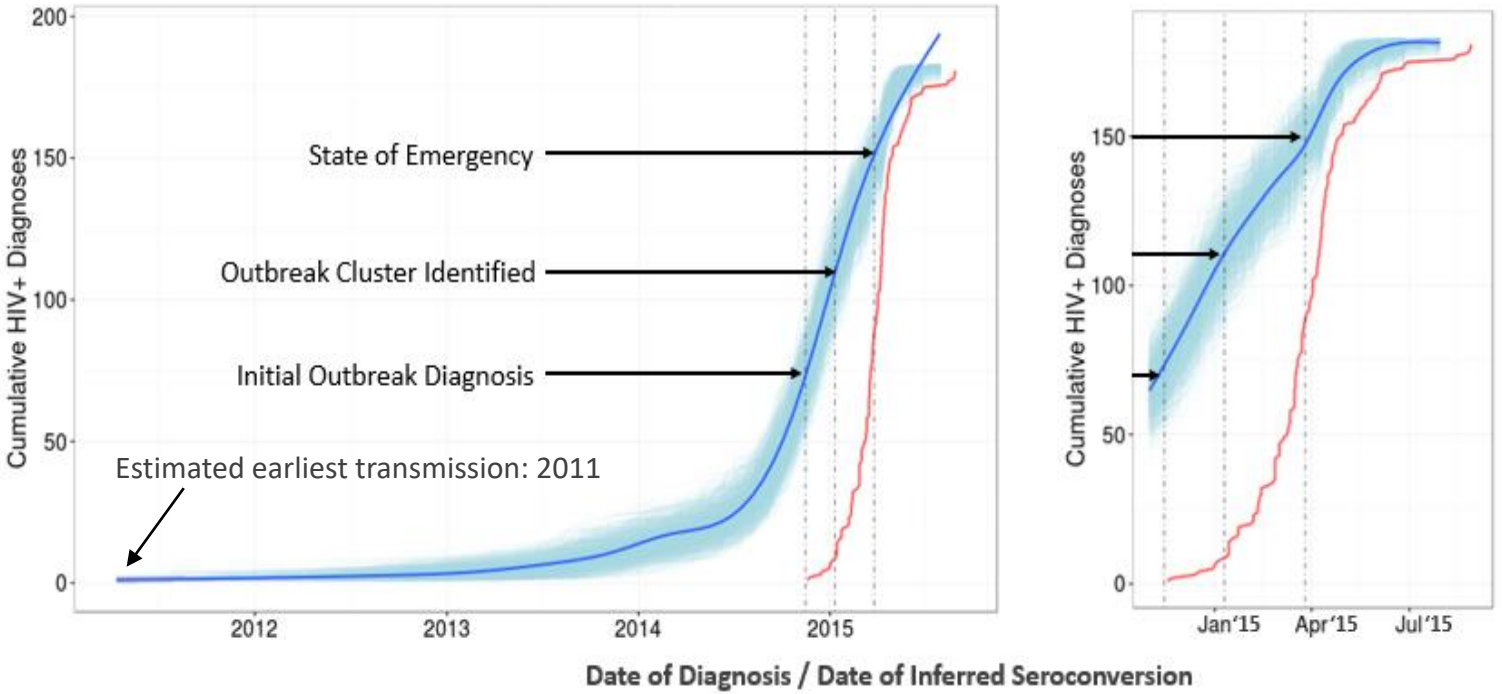
Transmission Cluster Investigation: Infer Transmission Network

Computationally combine reported epidemiologic data (e.g., contacts, transmission risk), genetic data, and inferred dates of seroconversion to model transmission network



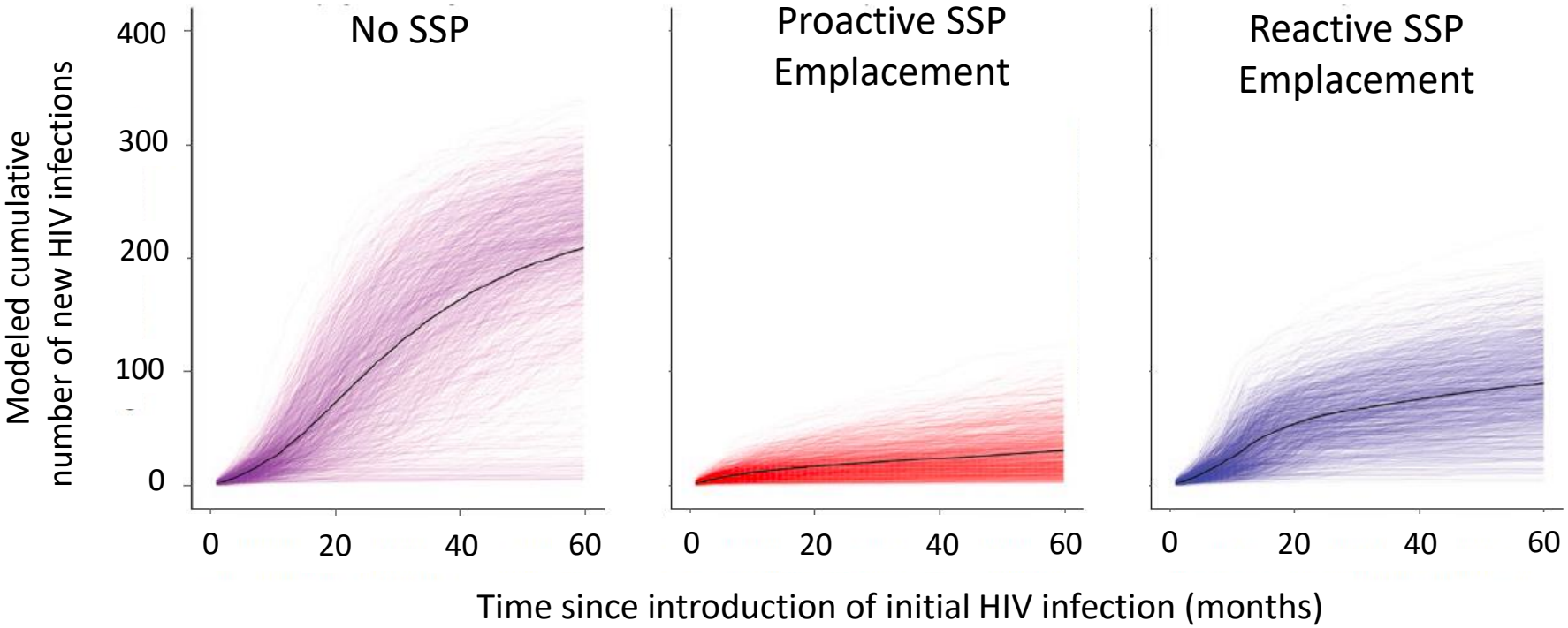
Campbell E. et al., J Infect Dis 2017; 216(9): 1053-1062

Transmission Cluster Investigation: Inferred Seroconversion Dates



Campbell E. et al., J Infect Dis 2017; 216(9): 1053-1062

Modeled Spread Infections
SSP Before HIV Introduction would Averted Most Infections



Goedell WC et al., Clin Infect Dis 2019; published online May 30

Indiana 2015 HIV Outbreak
Qualitative Study of Drug Use Practices

Why Did HIV Infection Spread So Rapidly?

Methods

- Data Collection: June-September, 2015
  - Sampled adults from SSP, by street recruitment, and by peer-to-peer
  - Interviewed in local church and SSP site for privacy
  - 4 focus groups (31 individuals) and 25 private interviews (25 individuals)
  - Audio-recorded interviews and interview notes transcribed
  - Thematic review* of OPANA® ER preparation and injection practices.

* NVivo 10 software, QSR International

Characteristics of Interviewees

	Focus Groups (n=31 persons* in 4 groups)	Private Interviews (n=25 persons)
Age, years	30-39 (59%)	median 33 (range 19-57)
White, non-Hispanic	29 (100%)	25 (100%)
Female	16 (52%)	11 (44%)
Enrolled in SEP	27 (90%)	19 (76%)
HIV-positive**	17 (57%)	10 (40%)
HCV-positive**	28 (90%)	21 (84%)
Drug use	Drugs injected	Primary drug injected
	• Any drug, past week 31 (100%) • OPANA® ER, past year 30 (97%)	• OPANA® ER 22 (88%) • OPANA® IR 1 (4%) • Methamphetamine 2 (8%)

* Percentage calculated from among respondents (e.g., 3 non-responders regarding race/ethnicity)

** By self report

Key Finding #1:
Frequent Injection Episodes with Multiple Injections

- Most participants who injected OPANA® ER reported injecting often
  - 3-7 injection events times per day
  - 2-4 injections per injection events
  - Typically shared a quarter of a pill with 2-4 injection partners
- Practice reported to be common among PWID in the community

Key Finding #2:
Users “Browned” OPANA® ER for Injection

- INTAC®, a proprietary high-molecular-weight polyethylene oxide, added to OPANA®ER during reformulation in 2012:
  - Deterrent to prevent crushing and insufflation
  - Forms viscous gel in aqueous environment that slowly releases drug through diffusion and erosion during gastrointestinal transit
- Users in Scott County applied moderate heat to “brown” OPANA® ER tablets to facilitate dissolution in water and reduction in gelling

Key Finding #3
Several Themes Related to Reformulated OPANA® ER Associated with Injecting the Drug and Injecting Often

1. Opioid potency and duration of action
2. Deterrent to prevent crushing and insufflation
3. Gelling capability to extend gastrointestinal release
4. Rinse shots
5. Economics of supply and demand

Opioid Potency: Analgesic Equivalency

Drug*	Route of Administration		Duration of action
	Oral, mg	Parenteral, mg	
Morphine	30	10	3-4 hours
Hydromorphone	7.5	1.5	3-4 hours
Oxymorphone	10	1.0	3-4 hours

* parenteral equivalency for oxycodone and hydrocodone not available, oral equivalency for fentanyl not available

Adapted from Gordon DB, Stevenson KK, Griffie J, et al. Opioid equianalgesic calculations. J Palliat Med. 1999;2(2):29-218.

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Potency of Opioid

Increased potency of drug increased intensity of withdrawal symptoms

- *"Then after they took OxyContins off the market, then they came out with the OPANAs. Which was 10 times worse than that OxyContin. With like the intensity of the withdrawals."* (JZ08)
- *"I could not find any of the OxyContins and someone came to me with an Opana, and that's how I ended up doing Opana but I had a lot of people tell me 'Don't do Opana because a lot of people say you do it one time and you're hooked'. You'll be sick the next day so you'll have to get another one. And that's exactly what happened. I did one that night and the next morning I woke up and I just felt, I felt terrible. And so I had to get another one. You get hooked on 'em really fast, the Opanas. Very fast."* (DB08)

Potency of Opioid

Short duration of action increased need to inject frequently

- *But, the Opana don't last near as long as the other stuff…The feeling of Opana will last 30 minutes... [It takes 4 or 5 hours with the Opana before you are sick] and then you got to do it again, or you feel really bad again. If you don't do enough Opana, then in a couple hours, you feel really bad again and… [have to inject]. Inject 6,7,8 times but only like small amounts.”* (DB01)

* Text in brackets are added by the researchers based on the full narrative to make the individual quotes free-standing and understood without reading the entire interview.

Deterrent to Prevent Crushing and Insufflation

Inability to crush OPANA® ER cited as a reason to move to injection

- *" [I was] probably 24....I snorted the Opanas. It was when the government put the formula in where you had to cook them…. It pretty much forced me to have to inject really... If there was a possible way I could snort them, I'd rather snort than shoot."* (JZ04)
- *"I couldn't find Opanas or any other type of pain medicine to snort. It became almost non-existent. So I was turned on to shooting up. So that's pretty much how that went down. [That was a couple years ago. I hadn't injected before a couple years ago after I couldn't find anything to snort]. I couldn't handle the withdrawals… Opana [was the first drug I injected]... I was doing the OxyContin before, snorting OxyContin….when I was 18. I don't know, it was probably 23, 24 [when I first started snorting Opana] because they had a snortable kind before. "* (JD01)
- *"These [Opana ER] you can't. They're like, plastic. Real hard. Well, I shot too, but I, mostly I would snort it. But, and then, when you couldn't snort it at all. I started shooting it."* (JD02)

Gelling Compound to Extend Gastrointestinal Release

Presence of gelling capability increased the amount of solvent needed to adequately dilute diverted OPANA® ER tablets for injection

- *"You take a lighter and you melt it, because it gels up if you put water on it. It kills the gel in it, that way you can draw it up. It takes so much water, if you wanted to work the whole thing up, it would get so thick and be hard to draw up."* (DB03)
- *You can't get it all in one shot... you've got to put more [water] in there than what you can draw... You can get by with 120 units, but its real thick... It's real hard to draw up. You still have 50 left, and then even after that, you put more water on it and mix it some more because there's stuff left over.* (JZ05)

Rinse Shots

Users rinsed the cooker after the first injection (“rinse shot”) to create at least one more injection to ensure all drug was used.

- *“And then even after that [2 shots from a quarter of ER oxymorphone], you put more water on it and mix it some more because there's stuff left over. So, that's 3 shots right there. Just off a quarter piece. Some people rinse it more than once. They'll rinse it again. So, they're doing 4 shots.”*(FG3)

Rinse Shots

Rinse shots not common with other injected drugs

- *"If you've got decent dope [methamphetamine], you do a shot and you're good, you know. . . Heroin, I've seen people try to take, get three or four shots off of it, but you can't, you know, because heroin it's one shot and you're done."* (DB05)

Economics of Supply and Demand

Increasing price of diverted drug created pressure to inject together

- *"Well, if you buy, these pills, a whole pill is like 200 dollars if you buy it. And, we'd always, sometimes we'd have just enough [money] to get high for a quarter of a one. Sometimes 2 or 3 of us would do a quarter of a pill."* (DB05)
- *"There are sometimes, another person [I inject with]…And it's usually to help us because we can't make enough money to get that quarter, and it's usually like the first quarter of the day because I'm sick, I've only made maybe $20, I'm short $15. There might be another person that's short the other $20, so we'll all get together, throw our money in together, and then we'll go do the quarter three ways."* (JD01)

Summary of Drug Characteristics and Infection Risk

	Characteristic of drug		Increased infection risk
Opioids:	Addiction potential		
↓	Effect duration hours	→	More injection events per day
Oxymorphone:	Greater potency	→	More intense withdrawal
↓			
OPANA® ER:	Crush resistance	→	Users move to injecting drug
	Greater solvent need	❯	More injections per event
	Rinse shots		
	Higher cost	→	Increased equipment sharing

Why Did Users Persist in Using OPANA® ER Despite Decreasing Supply and Increasing Cost?

- **Predictable dosing and perceived as “safe” to use**
  - Produced under Good Manufacturing Processes (GMP)
  - Precise dosing (heroin may be variable)
  - Free of other drugs (no fentanyl)
  - Reduced risk of infectious contaminants (wound botulism)

Hepatitis C Virus (HCV) Outbreak, New York State, 2011
Association Drugs Injected and Risk for HCV Infection

Drug injected	Hepatitis C Status		p-value
	Reactive (n=34)	Nonreactive (n=66)	
Prescription opioids	26 (77%)	27 (41%)	<0.001
Heroin	9 (26%)	24 (36%)	0.32
Cocaine	9 (26%)	11 (17%)	0.25
Bath salts	7 (21%)	3 (5%)	0.01
Crack	2 (6%)	2 (3%)	0.49
Methamphetamine	2 (6%)	1 (2%)	0.23
Other	0 (0%)	8 (11%)	0.08

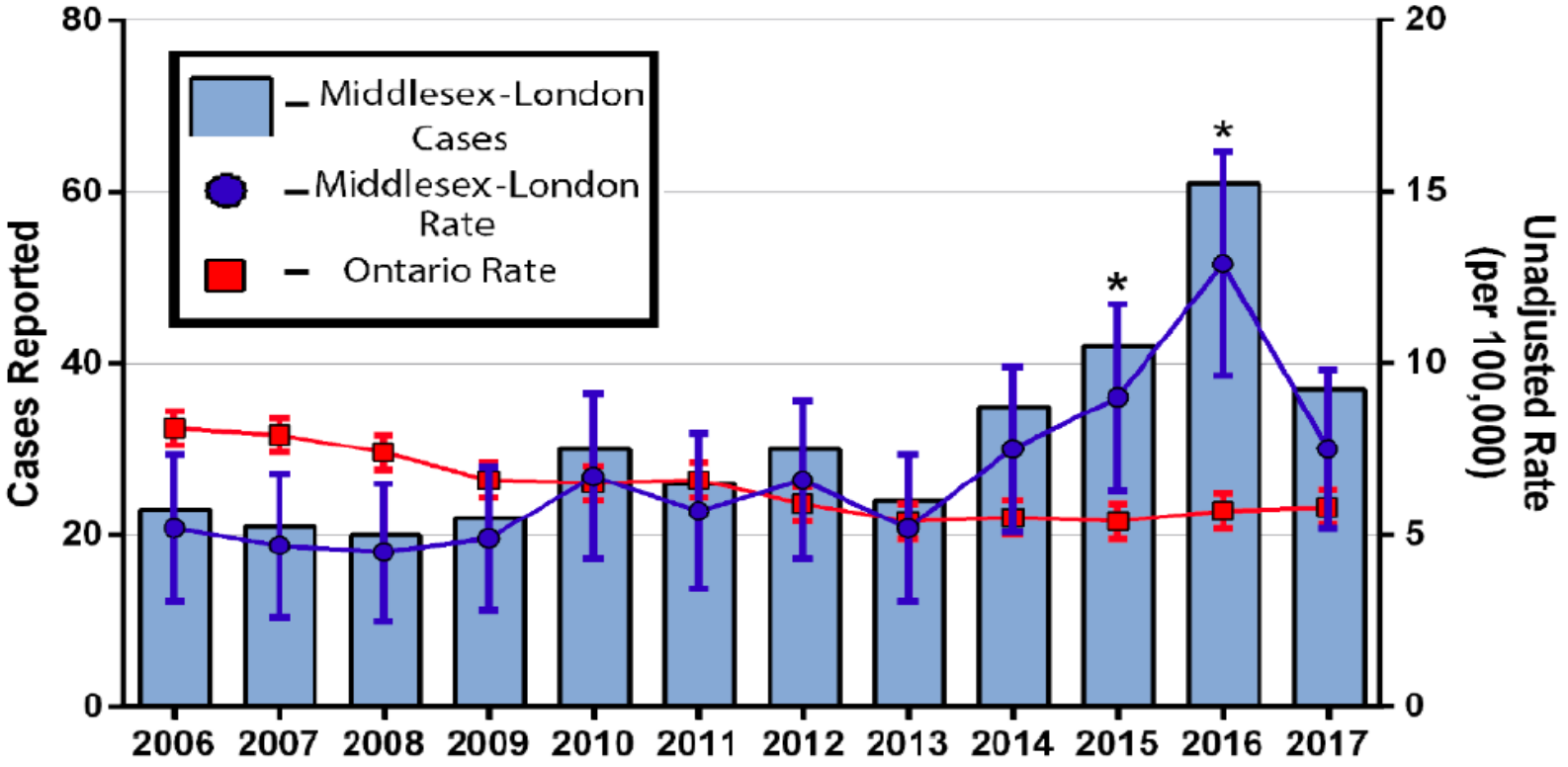
Zibbell *et al.* 2014, Am J Pub Health 104(11): 2226-2232

Hepatitis C Virus (HCV) Outbreak, New York State, 2011
Types of Prescription Opiates Injected

Prescription opioids	Number of persons reporting use
OPANA® (oxymorphone)	58 (61%)
OxyContin® (oxycodone)	21 (22%)
Dilaudid® (hydromorphone)	7 (7%)
Roxycontin® (oxycodone)	3 (3%)
Morphine	4 (4%)
Vicodin® (hydrocodone)	1 (1%)
Percocet® (oxycodone)	1 (1%)

Zibbell *et al.* 2014, Am J Pub Health 104(11): 2226-2232

HIV Outbreak Among PWID in London, Ontario



Ball et al., J Acquir Immun Deficien Syndr, 2019; published online April 19

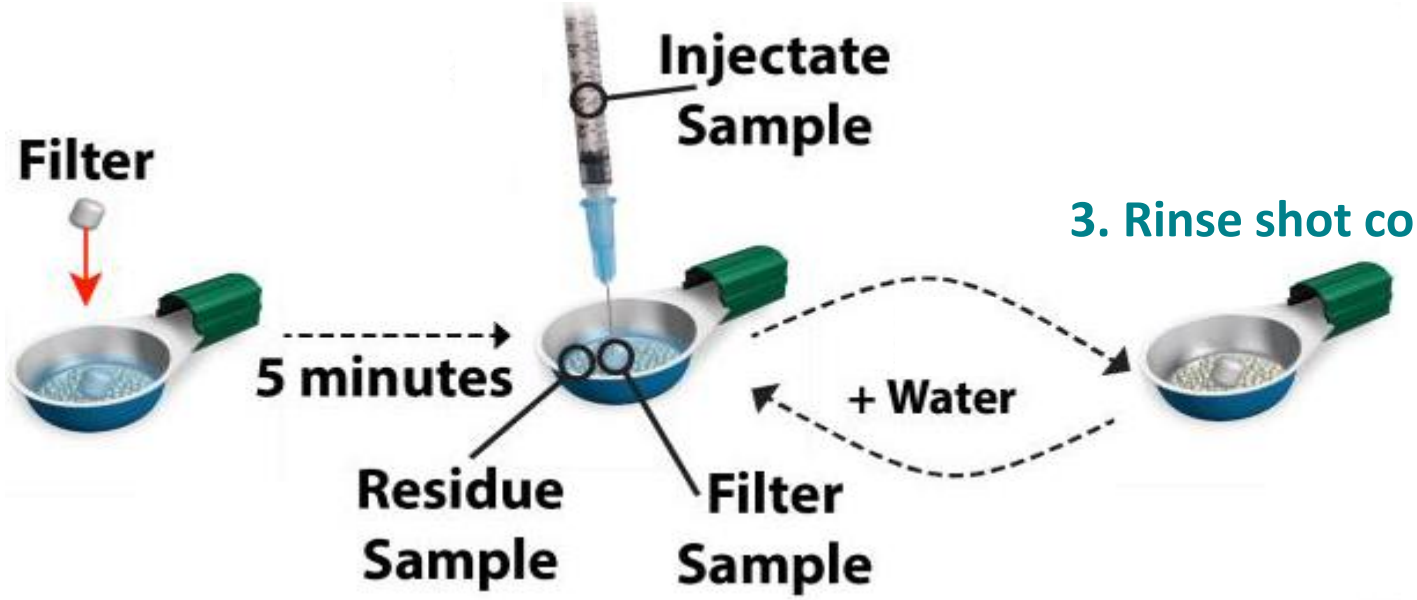
HIV Outbreak Among PWID in London, Ontario

- Highly resourced area for HIV prevention
  - Widespread SSPs with extensive harm reduction activities
- Preferred drug was controlled-release hydromorphone capsules
  - Manufactured with *microcrystalline cellulose*
  - Stabilizer in controlled-release drug formulations
  - This material supported persistence of HIV
- During drug preparation, microcrystalline cellulose drawn into filters, which were reused through “rinse shots”
  - Up to 45% of drug remained cooker and filter after first use
  - Drugs were prepared without heating

Ball et al., J Acquir Immun Deficien Syndr, 2019; published online April 19

HIV Outbreak Among PWID in London, Ontario

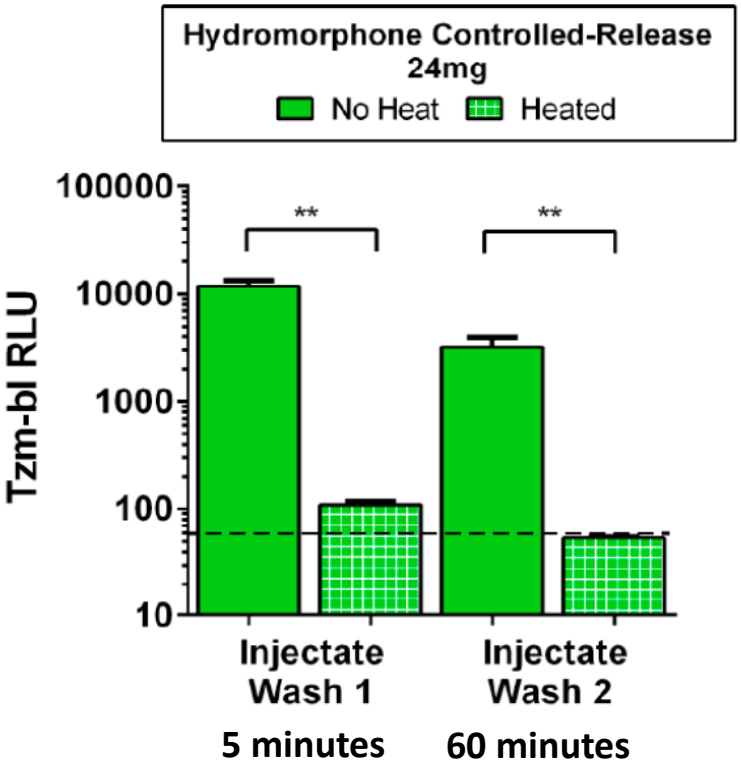
1. HIV introduced when originally sterile needle reused to prepare rinse shot



2. Microcrystalline cellulose preserves infectious HIV

Ball et al., J Acquir Immun Deficien Syndr, 2019; published online April 19

HIV Outbreak Among PWID in London, Ontario



- Replication competent HIV detected in washes up to 1 hour after initial use (dark green)
- Heating solution to a boil for more than 10 seconds reduced infectious HIV (light green)
- Risk for HIV transmission from additive to the drug was reduced by heating solution

Ball et al., J Acquir Immun Deficien Syndr, 2019; published online April 19

The Indiana HIV/HCV Outbreak: Implications for Prevention

- The United States is in the midst of an expanding epidemic of prescription opioid and heroin abuse with increasing use of methamphetamine

- This epidemic is generating a new population of PWID not traditionally considered vulnerable to HIV/HCV infections
  - Predominately rural with limited resources
  - Threatens to erode our substantial collective success controlling PWID-associated HIV infections

The Indiana HIV/HCV Outbreak: Implications for Prevention

- Injection drug use highly variable
  - In-depth interviews with PWID critical to understanding potential transmission pathways, and designing interventions and messaging to prevent outbreaks

- Numerous interventions have proven successful at reducing the risk of infection from unsafe injection of drugs (e.g., syringe service programs, medication assisted therapy, TasP, heat application to drug)
  - Models lacking how to operationalize these interventions in rural settings
  - Epidemiologic and clinical science can guide us to the right solutions

New CDC Resources About SSPs

www.cdc.gov/ssp

Effectiveness of Syringe Services Programs

Summary of Information on The Safety and Effectiveness of Syringe Services Programs (SSPs)

Syringe Services Programs (SSPs) Fact Sheet

Syringe Services Programs (SSPs) FAQs

Acknowledgments (the work does not end…)

- **Scott and Clark County Health Departments**
- **Scott County Sheriff's Office**
- **Foundations Family Medicine**
- **CEASe of Scott County**
- **Scott Memorial Hospital**
- **Indiana State Department of Health**
- **Indiana Family and Social Services Administration**
- **Indiana University**
  - School of Medicine
  - School of Public Health
- **Louisville 550 Clinic**
- **Centers for Disease Control and Prevention**
  - Division of HIV/AIDS Prevention
  - Division of Viral Hepatitis
  - Division of STD Prevention
  - National Center for Injury Prevention and Control
  - Office of Public Health Preparedness and Response
- **Health Resources and Services Administration**
- **Substance Abuse and Mental Health Services Administration**

Thank you!

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